

Graduate thesis

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## Are mirror movements associated with bimanual hand function among children with unilateral spastic cerebral palsy?

Graduate thesis in medicine

Supervisor: Torstein Vik, Professor. Lars Adde, Phd. Ann-Kristin Elvrum, Phd.

Trondheim, June 2016

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Norges teknisk-naturvitenskapelige universitet



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Science and Technology

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## Abstract

Children and adolescents with unilateral spastic cerebral palsy (USCP) may experience mirror movements (MM). The amount of MM may indicate differences in the organization of the cortico-spinal motor tracts, which may in turn affect the effectiveness of interventions aimed to improve hand function. However, it is unclear if MM affect bimanual hand function in this population.

### **AIM:**

This study aimed to assess whether MM affected bimanual hand function in children with USCP.

### **METHOD:**

Eligible to participate in this study, were children and adolescents with USCP. Children and adolescents were recruited from two sites: In Trondheim, Norway, a convenient sample of 18 children and adolescents (9 females; age range 12-20 y, mean 12.2 y) was recruited through the outpatient clinic. In Melbourne, Australia, further 18 patients with USCP participating in an on-going research project were recruited. Since the latter population, in several important aspects, turned out to be markedly different, from those recruited from the site in Trondheim, the present study was restricted to the Trondheim population. Bimanual performance was scored using the Assisting Hand Assessment (AHA), and manual capacity was scored using the Box and Block test (B&B). Mirror movements were scored clinically according to Woods and Teuber (W&T) based on video recordings. In addition, MM were assessed using a newly developed computer-based video analysis software. Mirror movements were then correlated with hand function.

### **RESULTS:**

When MM were scored according to W&T, moderate to high negative correlations were found between MM and all measures of hand function (Spearman's rho ranging from -0.50 to -0.66). When MM were measured using the computer-based method, only a low

to moderate negative correlation was found between MM and capacity (B&B) in the affected hand (Spearman's  $\rho = -0.50$ ).

***INTERPRETATION:***

Mirror movements in the affected and in the non-affected hand, affects bimanual performance and capacity in both hands negatively among children over the age of 10.

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# 1. Cerebral palsy

## 1.1 Definition

Cerebral palsy (CP) is an umbrella term, covering a group of permanent and non-progressive disorders of movement and posture caused by lesions or defects of the central nervous system (CNS) originating in the early stages of human development (before 2 years of age) (1). The diagnosis CP is however associated with much more than motor impairments. It is not an etiologic diagnosis, but a clinical diagnosis consisting of a heterogeneous group of disorders. Because of its complexity the definition has been a subject to discussion through history. In 2007 Rosenbaum and colleagues published a new definition of CP, representing the complexity of the diagnosis and its associated challenges (2):

*Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems (3).*

Because CP is caused by a lesion or defect to the developing nervous system, it is not uncommon that the injury affects other functions in addition to motor function. Typical associated impairments are reduced vision or hearing, eating disorders, growth disturbances, cognitive impairments and/or epilepsy (3).

## 1.2 Prevalence

Cerebral palsy is a major cause of childhood disability. The prevalence of CP ranges from 1.5 to 2.5 per 1000 live births, with little or no variation among western nations (4). The 2014 annual report published by the Cerebral palsy register in Norway (CPRN) showed a prevalence of 2.5 per 1000 live births, that had been stable over time (5). Recently a review including 49 studies showed an overall prevalence of 2.11 per 1000, also stable

over time (6). Another study, however, showed an overall decrease in prevalence of CP between the years 1980-2003, from 1.9 to 1.77 per 1000 live births (7).

### 1.3 Diagnosis and classification

Cerebral palsy can be a challenging diagnosis. Cerebral palsy constitutes of several possible neurological abnormalities that can have a variety of clinical presentations (8). Different signs, i.e. abnormal muscle tone, persistence of primitive reflexes and delay in reaching motor milestones, can lead to a suspicion of CP. It is a clinical diagnosis that can be established based on a physical examination performed by an experienced examiner. Genetic/metabolic disorders are important to exclude (8). There is an increasing trend towards early interventions, and a younger age for identification of high risk of CP is therefore desirable (8). Among premature with identifiable risk factors, early diagnosis of CP at 12 weeks of age is now possible based on an abnormal General Movements Assessment (a type of infant spontaneous movements) in combination with abnormal neuroimaging (9). In Norway the average age for CP diagnosis is 23 months, with a median age of 16 months (5). Children vary in their motor abilities, and it can therefore sometimes be difficult to draw a precise line between very mild CP and other motor abnormalities (8). In addition the neurologic system of the infant and young child is under development, and during the earliest years a variety of motor abnormalities may be transiently present and not necessarily evolve into CP. Even quite striking neurologic abnormalities found on examination in the first year of life can sometimes disappear (8). After recommendation from the Surveillance of Cerebral Palsy in Europe, the final CP diagnosis is set when the child is 5 years old and is determined after the child's dominating motor impairment (5). The degree of activity limitation should be characterized. It is not enough to label children with CP on the basis of an abnormal examination alone, without evidence of activity limitations (8).

Cerebral Palsy can be classified using different systems (3, 8). The two most common ways to classify CP is according to the type of motor abnormalities and their anatomical distributions. Based on the predominant neurologic impairment of the motor system, the SCPE groups CP into three: Spastic (87%), dyskinetic (7%) or ataxic (5%). The spastic subtype is further divided into bilateral and unilateral form (5, 8). This

classification system of CP, proposed by the SCPE, is today the most commonly used system in Norway. The International Statistical Classification of Diseases and Related Health Problems 10<sup>th</sup> Revision (ICD-10) (10) also classifies according to anatomical distribution in addition to neurologic impairment, but uses different terms regarding the anatomical subgroups. In most CP cases, three types of limb distribution predominate – hemiplegia (unilateral) and diplegia/quadruplegia (bilateral) (9, 10). Cerebral palsy can also be classified by severity or functional motor abilities (8). Tools exist to classify both gross and fine motor function. The Gross Motor Function Classification System (GMFCS) classifies ambulation in to five levels based on functional mobility and activity limitations (11). The Bimanual Fine Motor Function Scale (BFMF) and the Manual Ability Classification System (MACS) are used to classify hand function (3, 12). The Manual Ability Classification System will be described later in this thesis. Based on one or several of these systems, CP is divided into subtypes. The most common and preferred system today is to combine the anatomical distribution with the neurologic impairment, e.g. bilateral spastic CP.

#### 1.4 Pathogenesis

Leading causes of CP are related to congenital malformations of the CNS and vascular disturbances within the brain (13, 14).

During the first and second trimester, cortical neurogenesis predominantly takes place, characterized by proliferation, migration and organization of neuronal cells (13, 14). Brain pathology in this period is characterized by malformations. During the third trimester, and persistent into postnatal life, growth and differentiation events are predominant. Disturbances of brain development during this period mainly cause vascular lesions. The various brain regions are vulnerable at different stages of brain development. During the early third trimester, periventricular white matter is especially affected whereas toward the end of the third trimester, grey matter, either cortical or deep grey matter, appears to be more vulnerable (13, 14).

The major neuropathology originating in the early to mid third trimester is periventricular lesions, periventricular leucomalacia (PVL) or intraventricular

haemorrhage (IVH) (13). These make up the main lesion pattern in preterm children. Periventricular leucomalacia is characterized by periventricular white matter loss and ventricular dilatation with irregular borders. Intraventricular haemorrhages are usually graded from I-IV based on radiologic criteria. With subependymal haemorrhage only as the mildest form (I), and germinal matrix haemorrhage with ventricular dilatation and periventricular hemorrhagic infarction (PHI) as the most severe form (IV). MRI findings of PHI are characterized by porencephalic focal ventricular enlargement, often accompanied by some gliosis (13).

Changes are mainly focal in IVH and bilateral in PVL. The origin of PVL is related to inflammation, and causes could be perfusion failure, infection or both (13). If the injury is moderate, only the pyramidal tracts supplying the lower limbs will be affected, leading to diplegia. A bigger lesion, affecting more laterally, will likely affect the pyramidal tracts of the upper limbs and give rise to quadriplegia (15).

In children born prematurely the circulation system is immature. IVH most commonly originates from rupture of fragile blood vessels within the germinal matrix, supplying the ependymal tissue surrounding the lateral ventricles. The changes are mainly focal and thus leads to unilateral CP. Intraventricular haemorrhage can cause impaired venous drainage and a feared complication is post-hemorrhagic hydrocephalus (15).

#### **1.4.1 Risk factors**

The causes leading to CP are poorly understood, but several risk factors are described. Cerebral palsy is a heterogeneous condition probably with many different causes. Traditionally the timing of an insult and subsequent brain injury responsible for CP is defined as being prenatal, perinatal or postneonatal in origin. Epidemiological studies have shown that as much as 70-80% of CP cases are acquired prior to labour/during fetal development (16). Risk factors for CP are multiple and rarely alone, but acting together to make a disturbance more likely. The main prenatal factors related to CP are: Preterm delivery, intrauterine growth restriction, intrauterine infections, multiple pregnancies, congenital malformation, ischaemic stroke, male sex and genetic factors (17, 18). In the next paragraphs some of these factors will be briefly addressed, followed by a short address on intrapartum asphyxia and postneonatally acquired CP.

### *Prenatal factors*

Preterm delivery is a major risk factor and is seen in about 35% of all cases. The lower the gestational age, the higher the risk is. The prevalence is highest in children born gestation week 28 or below, and declines with increasing gestational age (GA) (17). Whether prematurity is the sole cause of CP, or if both being born early and developing CP are caused by the same prenatal insult or genetic abnormality, is however unclear (19).

There is an association between inflammation of the foetal membranes (chorioamnionitis) and CP (20). One proposed mechanism is that the ascending infection reaches the decidua and triggers the maternal inflammatory system and the production of proinflammatory factors, such as cytokines and interleukins (21). Microorganisms and their products can also reach the fetus, and cause a fetal inflammatory response. The proinflammatory factors may cause damage to the developing brain and lungs, and lead to preterm delivery. The inflammatory response inhibits oligodendrocytes in the developing white matter and thus ultimately leads to CP (21).

Congenital malformations and CP are highly associated (22). Children with CP have a 4-6 times higher rate of congenital malformations than the average population. Cerebral malformations are most common (overall, 8.6% of all children with CP are diagnosed with cerebral malformation), but they can also be non-cerebral or related to chromosomal anomalies. Garne et al. found that 12 % of children with CP also were diagnosed with congenital malformations. The most frequent types of cerebral malformations are microcephaly and hydrocephaly. Children with cerebral malformation have a higher GA at birth than children with CP without malformations. Children born at term have a significantly higher prevalence of cerebral malformation, compared to children born before week 32 (22).

### *Perinatal factors*

For decades, birth asphyxia was believed to be the predominant aetiology of CP. Birth complications, including asphyxia, are now considered as minor factors, estimated to account for about 6% of patients with congenital cerebral palsy (16).

### *Postneonatal factors*

In about 10-20 % of patients, cerebral palsy is acquired postnatally, mainly because of brain damage from bacterial meningitis, viral encephalitis, hyperbilirubinemia, motor vehicle collision, falls or child abuse (16).

## **2. Unilateral spastic CP**

In this thesis, my focus is upon the subtype unilateral spastic CP (USCP). Unilateral spastic CP is seen in about 40% of all children with CP (5).

In most children with USCP, the upper limb is more severely affected than the lower limb (15, 23). In a population-based study from Sweden performed by Carnahan and colleagues, the distribution of GMFCS and MACS scores among the different subtypes of CP were investigated (23). The study found manual ability to be more limited than cross motor function among children with USCP. As a consequence, a person with unilateral CP will probably walk, or try to walk, but will sometimes not use the affected arm at all, leading to a lack of bimanual function (23).

In addition to generally having a lower GMFCS score (i.e. better walking abilities) compared with the group of children with spastic bilateral CP (23), children with USCP also seem to have fewer associated impairments (24). In a study performed by Andersen et al., only 72% of all children with CP had normal or understandable speech, whereas 90% of the children with USCP had normal speech. The children with USCP also had lesser amount of active epilepsy, better vision and a lesser proportion mental retardation (24). In other words, children with USCP seem to be mostly affected by their hand function.

## **2.1 Hand function among children with USCP**

Children with USCP, have one hand that functions well, while the other has some degree of dysfunction. Impairments in hand function generate restrictions in daily-life activities and self-care (25). Most activities are dependent on the ability to use both hands together (26). Simple things such as tying shoelaces, making a sandwich or taking money out of a purse can be difficult to manage with only one hand. The degree of the impairments, is therefore an important determinant for participation in daily-life activities (26).

There are several approaches to upper limb therapy in children with USCP (27). One of the most extensively investigated approaches is constraint-induced movement therapy (CIMT). The method consists of immobilization of the non-affected hand, combined with individualized, intensive repetitive training of the affected hand (27).

## **2.2 Classification and assessment of hand function among children with USCP**

Hand function is important for performance of daily-life activities, it is therefore important to have methods to classify and measure hand function. Measuring of hand function is also important when it comes to planning and evaluation of treatment. The Manual Ability Classification System (MACS), the Assisting Hand Assessment (AHA) and the Box and Block test (B&B) are such tools, and will be described in the next paragraphs. Following this, factors that can affect hand function will be mentioned and one of them will be described in more detail.

### **2.2.1 The Manual Ability Classification System**

The Manual Ability Classification System, classifies into five levels how children with CP use their hands to handle objects in daily activities (28). Level I include children with minor limitations, while children with severe functional limitations are found at levels IV and V. MACS does not describe the function of each hand separately, or their best capacity, but rather the children's overall ability to handle everyday objects. In order to obtain knowledge about how a child handles various everyday objects, one has to ask someone who knows the child well. MACS can be used for children aged 4-18 years (28).

### **2.2.2 The Assisting Hand Assessment**

The Assisting Hand Assessment, developed by Krumlinde-Sundholm and Eliasson in 2003, measures the effectiveness, of with which a person with USCP makes use of his/her affected hand in bimanual performance activities (26). AHA is based on recognising that the two hands play different roles, and that an assisting hand not necessarily need to be as quick and as manipulative as a dominant hand, to effectively assist in bimanual task performance (29).

AHA is based on observations of actions performed in an activity that is relevant and motivating for the individual (30). The intent is to reflect the performance, not the best possible capacity (29). The person is video recorded in a standardised manner, while performing age appropriate bimanual activities, such as playing a board game with toys from the AHA test kit (for children up to 12 years of age), or making a sandwich (for adolescents from 14 years of age) (30). By review of the video, the most representative performance is scored by a certified rater, in line with the criteria specified in the AHA manual (30).

AHA has been found to be valid and reliable for children and adolescents between 18 mnd and 12 years. There is a low association between AHA measures and age, suggesting that age may be of minor importance (29).

### **2.2.3 The Box and Block test**

The Box and Block test measures gross manual dexterity, and can be used to compare the gross manual dexterity between the affected and the non-affected hand in individuals with unilateral CP (31). The test measures the child or adolescents manual capacity. In the test, the child or adolescent is instructed to move as many cubic blocks as he or she can between two partitioned compartments in a box. The subject's score is the number of cubes transferred in one minute. The Box and Block test has norm scores for typically developed children and adolescents between 3 and 19 years of age, in addition to adults (31-33). Older children transfer significantly more blocks than younger children (31-33).



### 2.3 Mirror movements

Several factors have been suggested to affect hand function. In addition to spasticity, muscle weakness and sensory deficits, the occurrence of mirror movements (MM) has also been suggested to interfere with hand function, especially bimanual performance (34).

Mirror movements are unintentional, symmetrical movements of one side of the body, which mirror voluntary movements of the contralateral side (35, 36). They are known to predominantly affect the distal upper limbs. Because of their symmetrical nature, MM can cause difficulties in performing asymmetrical daily-life activities (35).

Physiological MM are present in newborn infants, show a steep decrease in early childhood, and disappear after 10 years of age (37). Mirror movement after childhood may be a sign of pathology, and should be investigated (35). Some children and adolescents with neurological disorders like CP, in particular those with unilateral spastic subtype, experience sustaining MM (36, 38).

The physiological MM in early childhood can be explained by the inhibition hypothesis: Before the age of 10, the corpus callosum and the pyramidal system is immature. After maturation, the corpus callosum mediates a two-way inhibitory system thorough which each hemisphere supresses the contralateral hemisphere's ipsilateral projecting pyramidal system (39).

Various mechanisms have been proposed to explain the occurrence of pathological MM (35). One is the one-way inhibition hypothesis: The inhibitory system of the intact hemisphere will mature, while the inhibitory system emanating from the damaged hemisphere will not (39). The one-way inhibition hypothesis predicts that the intact hemisphere, via transcallosal inhibition, supresses MM emanating from the damaged hemisphere to the good hand. The damaged hemisphere will however not supress MM from the intact hemisphere and MM in the impaired hand will persist unsuppressed (39). This hypothesis however, fails to consider reorganization of the CNS after an early unilateral lesion. One reorganization mechanism is the bilateral branching of axons from the same cortical motor region to homologous motor neuron pools on both sides of the

spinal cord – meaning that both hands shares the same common cortical representation (40). Another reorganization theory is that the pyramidal tract from the intact hemisphere persists to exist and becomes hypertrophied, and in addition the pyramidal tracts from the damaged side degenerates (39). Early in human development, the corticospinal tract has more extensive contralateral and ipsilateral projections than in maturity (41). Normally the ipsilateral projections withdraw gradually until the age of two, and mostly contralateral projections remain. When one hemisphere is injured, however, the ipsilateral projections supplying the affected limb will persist, and the crossed projections will disappear (41). The hypertrophied tract consists of both crossed and uncrossed pyramidal tract fibres from the intact hemisphere, innervating the normal and the impaired limbs respectively. This increase in ipsilateral fibers may trigger MM in the impaired hand when the intact hand performs a task (39).

Lesion timing is an important factor for MM. Children with early lesions (periventricular white matter lesion) shows more MM compared to children with lesions that occur after birth (42). Early lesions are more likely to give rise to structural reorganisation of the CST, resulting in ipsilateral control of the paretic side. In these children, motor function may be maintained through the ipsilateral connections, though at the expense of producing MM (40). Hence, the earlier a lesion occurs during the prenatal and perinatal period, the better is the prognosis regarding hand motor abilities in general (14). Normal hand function, however, seems possible only with preserved crossed corticospinal projections from the contralateral hemisphere (14).

### **2.3.1 Assessment of mirror movements**

#### ***Woods and Teuber***

Woods and Teuber (W&T) developed in a 1978, a scale to classify mirror movements qualitatively (36). It remains the most commonly used method for classifying mirror movements in children with unilateral cerebral palsy. When seated, the child is asked to perform three unimanual activities that are video recorded: Opening and closing of the fist (task 1), finger opposition (task 2), and tapping of fingers on the examination board (task 3). The intensity of visible mirror movements are assessed using a five-level scale: 0) no clear imitative movement, 1) barely discernible repetitive movement, 2) slight

mirror movements, or stronger, but briefer repetitive movements, 3) strong and sustained repetitive movement, 4) movement equal to that expected for the intended hand. The scores from each task are then added together, creating the possible total score range from 0 to 12 (36).

### ***Motion capture technologies***

Our group recently developed a new method to assess MM quantitatively, using motion capture technologies (unpublished work by Neergård). Motion capture technologies provide the possibility to quantify human movement based on objective criteria. Computer vision systems can provide description and understanding of human movement from image sequences.

Jensenius and co-workers developed a software collection, the Musical Gesture Toolbox (MGT), for performing video analysis of music-related movements and gestures in musicians and dancers (43). For the purpose of studying quality of General Movements and early prediction of CP in high-risk infants, Adde et al. customized the MGT into the General Movement Toolbox (GMT) (44). The General Movements Toolbox has been described elsewhere (44). Briefly described, a motion image is calculated based on subtracting subsequent frames in the video stream. Quantitative data representing movements in the video can be exported based on pixel values in the motion image (this will be described in more detail later in this thesis). The newly developed method using computer-based video analysis to quantify MM is based on the GMT developed by Adde et al.

## **2.4 Is there a relationship between mirror movements and hand function?**

Results of studies addressing this question have been inconsistent. Some studies have reported that mirror movements may affect bimanual performance in children with USCP (34, 38, 42, 45), while another study could not show such an effect (46). Results have also been inconsistent regarding whether MM affect manual capacity (42) or not (34, 38). The discrepancies and the contradictory results reported, may in part be due to how MM are assessed. Currently these movements are assessed qualitatively with subjective ratings (W&T). The contradictory results regarding the relationship between

hand function and MM may therefore in part be due to the use of qualitative tools to assess MM. The new method developed by our group to assess MM quantitatively using computer-based video analysis, may be a useful tool in this respect.

### **3. Aims**

The primary aim of this study, was to investigate the association between hand function in individuals with unilateral spastic CP, and MM assessed according to W&T. Secondary aims were, to investigate if our recently developed method to quantitatively assess MM using computer-based video analysis could detect an association between MM and hand function.

Our primary hypothesis was that a high amount of MM is associated with more impaired hand function. Our secondary hypothesis was that a similar association could be detected if MM were assessed using the computer-based video analysis method.

### **4. Methods**

#### **4.1 Study design**

Eligible to participate in this study, were children and adolescents with unilateral spastic CP. Mirror movements (MM) were scored based on video recordings according to Woods and Teuber (W&T) (36). Mirror movements were also quantified using a computer based video analysis program, described by Adde et al. (44, 47). Hand performance was measured using the Assisting Hand Assessment (AHA) developed by Krumlind-Sundholm and Eliasson (26). Manual capacity was assessed with the Box and Block test (B&B) (31). The amount of MM measured with both methods, were then correlated with the AHA and the B&B.

#### **4.2 Participants**

Children and adolescents diagnosed with unilateral spastic CP, according to the guidelines proposed by the European Network for the study of CP (SCPE) (1), and mentally able to cooperate, were invited to participate in this study. The children and adolescents were recruited from two different study sites: The outpatient clinic at St. Olav University Hospital, Trondheim, Norway (autumn 2011), or through their participation in the research project "Cognition and Bimanual Performance in Children

with Unilateral Cerebral Palsy” at Monash Children’s Hospital, Melbourne, Australia (autumn 2015). Ethic committees, or boards at both sites approved the study.

Criteria for exclusion were upper limb surgery during the preceding 12 months, and/or injections of Botulinum toxin-A during the preceding 3 months before the study.

In Trondheim, 46 children and adolescents were invited to the study. Twenty-one of them agreed to participate. Of these, 19 met for examination. One of the participants who met for examination, had to be excluded because of technical difficulties with the video recordings. In Melbourne, 21 patients were invited to join the study. Nineteen accepted the invitation, and all of them met for the examination. One of the participants from Melbourne was also excluded from the study because of technical difficulties. Thus, 36 children and adolescents participated in the study, 18 from Trondheim and 18 from Melbourne (**table 1**).

**Table 1:** Background information. Children with unilateral spastic cerebral palsy included in this study, recruited from two different study sites.

		<b>Trondheim</b>	<b>Melbourne</b>
<b>Participants</b>		n = 18	n = 18
<b>Sex</b>	female	9 (50 %)	12 (67 %)
<b>Age</b>	mean (range)	15.7 (12-20)	9.8 (6-14)
<b>Affected side</b>	right	9 (50 %)	14 (78 %)
<b>GMFCS*</b>	1	9 (50%)	11 (61%)
	2	9 (50%)	7 (39%)
<b>MACS**</b>	1	2 (11 %)	3 (17 %)
	2	14 (78 %)	15 (83 %)
	3	2 (11 %)	0

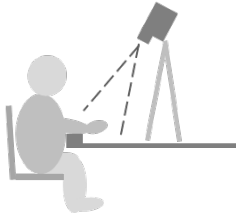
\*Gross Motor Function Classification System. \*\* Manual Ability Classification System

## 4.3 Assessment of mirror movements

### 4.3.1 Provoking mirror movements

The videos were recorded using a Sanyo VPC-HD2000 camera, placed orthogonally above the participants (**figure 1**).

*Figure 1: Video recording setup.*



The participants were placed in a comfortable sitting position on a chair resting their forearms on an examination board, with free space to move their arms. They were allowed to practice the tasks. Instructions were given to perform three repetitive tasks: Opening and closing of the fist (task 1), opposition of index finger and thumb (task 2), and tapping their fingers on the examination board (task 3) (38). All tasks were performed separately for each hand, while resting the other hand on the examination board. The participants were asked to perform the three tasks first at their preferred speed (slow) and then as fast as possible. Each task lasted 15 seconds. All tasks were video recorded for later analyses. We decided to only analyse the video recordings from task 1, due to the large amount of data recorded and the limited amount of time available for this thesis.

### 4.3.2 Clinical evaluation of mirror movements

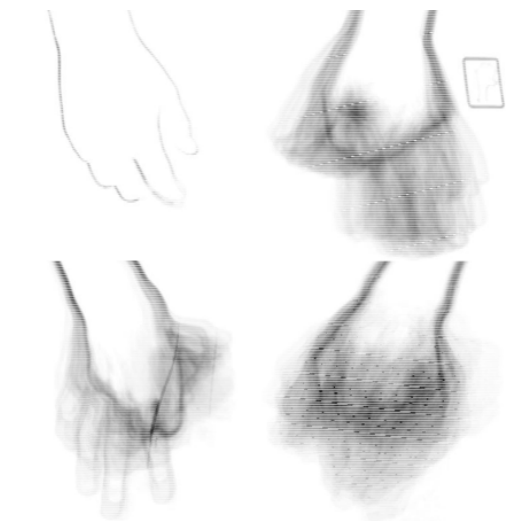
Two observers, an occupational therapist and a M.Sci in Human Movement Science observed the videos for MM activity in the resting hand, and scored them according to the classification proposed by W&T (36). The videos were presented to the two observers in random order. Only the hands of the participants were visible on the videos, and the identities of the participants were anonymized. The two observers first scored the videos independently. The final scores were then decided by the two reviewers in consensus and without knowledge of the following computer based video

analysis. The independent scores by the two observers suggested good interrater reliability of the W&T (weighted kappa varying between 0.81-0.89).

#### 4.3.3 Computer-based video analysis of mirror movements

The original video recordings were cut into 10 seconds sequences containing task 1 performed with both hands, and at both speeds, generating a total of 4 videos. To be able to analyse MM in both hands separately using the computer-based video analysis program, the four films were further cropped into two approximately equally sized frames, showing only one hand at a time, generating a total of 8 videos.

**Figure 2:** Screenshot of the computer-derived motion image. The participants were instructed to perform task 1 with their left hand, and at their preferred speed. Pixels displayed in white indicates no movement between the last frames, pixels displayed in black represents movement. Top: Participant *without* mirror movements in their right hand, clinically assessed to have a Woods and Teuber (W&T) score of 0. Bottom: Participant *with* mirror movements in their right hand, clinically assessed to have a W&T score of 2.



Identifying the change for each pixel between two frames in a video creates a motion image (**figure 2**). In a motion image, each pixel represents a point value of 0 and 1, 0 being white and representing no movement, and 1 being black and representing movement. The motion image provides the data for further qualitative and quantitative analyses (44). The computer-based video analysis software used to quantify MM provides us with several variables, describing motion in the image. In another study (unpublished work by Neergård) we found that the variable Quantity of Motion mean



(QoM) performed at slow speed, had a high correlation (Spearman's  $\rho = 0.72$ ,  $p < 0.01$ ) with W&T among children with USCP. This study therefore uses QoM as a measure for MM quantified using the computer-based video analysis software. Quantity of Motion is calculated as the sum of all pixels that changes between frames in the motion image, divided by the total number of pixels in the image. Quantity of Motion can be used as an estimate of movement in a video sequence (44).

## **4.4 Assessment of hand function**

### **4.4.1 Bimanual performance**

In this study, the AHA was used to evaluate bimanual hand performance. The School-Kids version of the AHA was used for children between 6 and 12 years of age. The Ad-AHA sandwich version was used for adolescents. The tests were administered and video recorded according to the AHA-manual (30).

The videotapes were scored by a certified occupational therapist and without knowledge of the MM scores and the B&B scores. The Norwegian participants (examined in 2011) were scored using the AHA 4.4. The Australian participants (examined in 2015) were scored using the newest version of AHA, the AHA 5.0. Both versions use a 4-point rating scale, but there is a slight difference concerning the scoring items. The AHA version 4.4 and AHA version 5.0 can, however, be compared and converted into a logarithmic scale, using a score conversion table (48).

### **4.4.2 Manual capacity**

The Box and Block test was used to evaluate hand capacity. The child or adolescent was instructed to move as many 2.5 cm blocks as they could in one minute, one-by-one, from one side of a box, over a low partition, to the other side of the box. The subject's score is the number of cubes, he or she, was able to transfer in one minute (31)

## **4.5 Statistical analysis**

Statistical analyses were performed using IBM SPSS version 23 (IBM, Armonk, NY, USA).

Normal distribution was evaluated using Q-Q plots and histograms. Linearity was explored through scatter plots. Bivariate correlations, using Pearson's rank, were performed between bimanual function (AHA) and manual capacity (B&B), and between each of these assessments and QoM. To study the association between W&T and hand function (AHA and B&B), Spearman's rho was calculated. As proposed by Portney and Watkins (49), correlation coefficients between 0 and 0.25 were considered to indicate little or no relationship, between 0.25 and 0.50 low, between 0.50 and 0.75 moderate to good, and above 0.75 were considered to indicate a good to excellent relationship. Portney and Watkins do however suggest that these limits not are meant as strict lines, but rather as guidance (49). Two sided p-values <0,05 were considered to indicate statistical significance.

To explore if there was a difference between MM measured in the affected hand and MM measured in the non-affected hand, Wilcoxon signed ranks test was used when MM were assessed according to W&T and paired Student's t-test was used when MM were measured using the computer-based method (QoM).

## 5. Results

During the analyses, it turned out that the children recruited in Trondheim and in Melbourne, differed significantly on a number of essential variables (**table 1 and appendix**). The main differences were that the children in Melbourne, compared with the participants in Trondheim, were significantly younger (**table 1**), had significantly poorer hand function and had very little variations in scores derived from both hand function tests, and in the amount of MM scored according to W&T (**appendix**). We therefore found it inappropriate to merge the two populations, and only the results from the participants in Trondheim will be presented in the following sections (the reasoning behind this decision will be further presented in the discussion).

### 5.1 Hand function

The results of the Assisting Hand Assessment (AHA) and the Box and Block test (B&B) are presented in **table 2**. There was a high positive correlation between bimanual performance (AHA) and hand capacity in the affected hand (B&B) (Pearson = 0.92,  $p < 0.01$ ), whereas there was no correlation between bimanual performance and hand capacity in the non-affected hand.

*Table 2: Hand capacity assessed using the Box and Block test (B&B) and bimanual performance assessed with the Assisting Hand Assessment (AHA) among children with unilateral spastic cerebral palsy.*

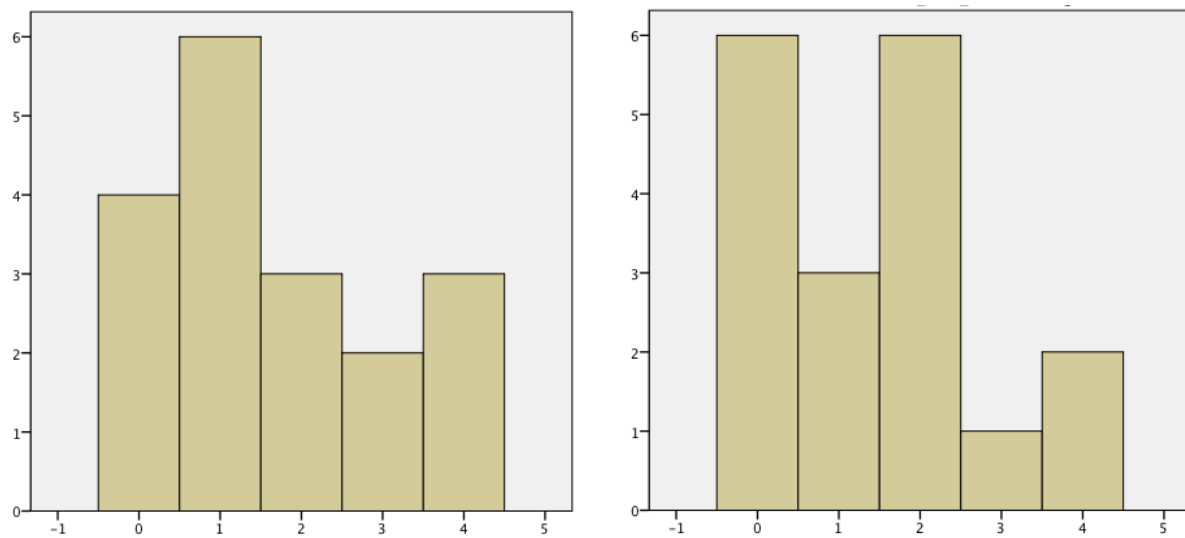
<b>AHA</b>	mean (SD)	n = 18 66.2 (16.8)
	range	37-100
<b>B&amp;B affected</b>	mean (std)	n = 17 28.4 (14.2)
	range	6-55
<b>B&amp;B non-affected</b>	mean (std)	n = 17 59.2 (9.9)
	range	46-87

## 5.2 Mirror movements

### 5.2.1 Mirror movements - Woods and Teuber

The distribution of the Woods and Teuber scores (W&T) is shown in **figure 3**. Eight participants (45 %) had MM (i.e. W&T score 2-4) in the affected hand, while nine (50 %) had MM in the non-affected hand (**figure3**).

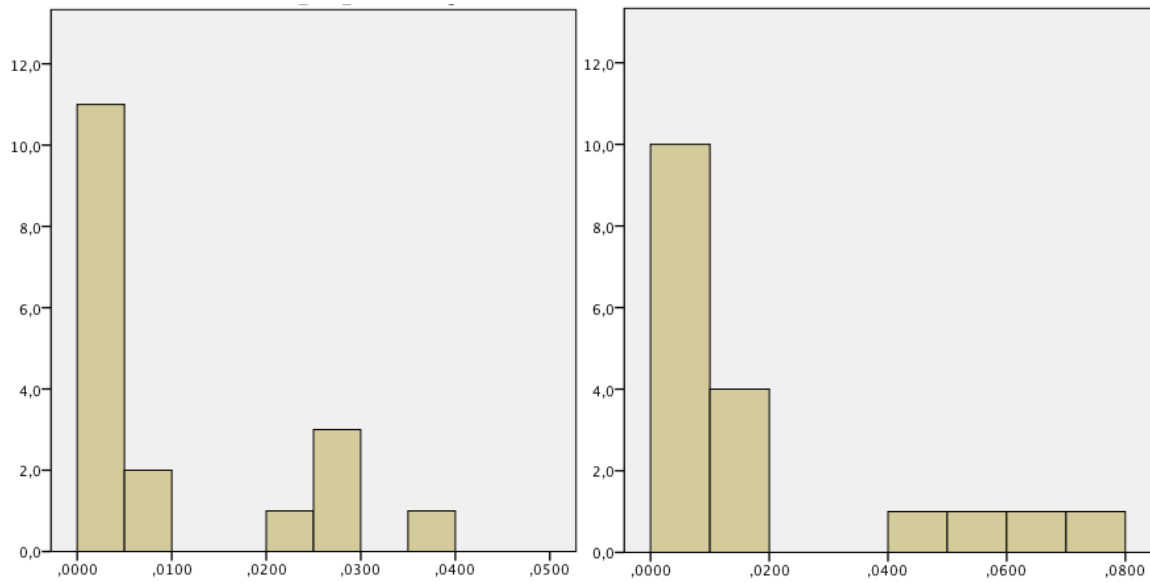
**Figure 3:** Distribution of mirror movements in children with unilateral spastic cerebral palsy assessed according to Woods and Teuber. Left: Affected hand (median = 1). Right: Non-affected hand (median = 1.5).



### 5.2.2 Mirror movements – Computer-based video analysis (QoM)

The distribution of MM assessed by the computer-based video analysis software (measured as Quantity of Motion (QoM)) is shown in **figure 4**. The mean score in the affected hand was 0.010 (SD: 0.013), while it was 0.007 (SD: 0.010) in the non-affected hand, the difference in MM between the two hands was however not significant ( $p = 0.129$ ). In the affected hand, none of the children had scores above 0.04, whereas in the non-affected hand, four of the children had scores above 0.04 (**figure 4**).

**Figure 4:** Distribution of mirror movements in children with unilateral spastic cerebral palsy measured in Quantity of Motion using the computer-based method. Left: Affected hand. Right: Non-affected hand.



### 5.3 Correlations between hand function and mirror movements

#### 5.3.1 Mirror movements assessed with W&T

Moderate to high negative correlations were found between MM and bimanual performance (AHA). Moderate to high negative correlations were also found between MM and hand capacity in the affected hand (B&B), whereas there was no correlation between MM and capacity (B&B) in the non-affected hand (**table 3**).

**Table 3:** Correlations between hand function and mirror movements assessed according to Woods and Teuber (W&T). Shaded areas represent statistical significant correlations.

	W&T affected		W&T non-affected	
	Spearman's rho	p-value	Spearman's rho	p-value
<b>AHA (n = 18)</b>	-0.65	0.004	-0.50	0.034
<b>B&amp;B affected (n = 17)</b>	-0.66	0.004	-0.59	0.013
<b>B&amp;B non-affected (n = 17)</b>	-0.10	0.711	-0.15	0.574

#### 5.3.2 Mirror movements assessed with QoM measured by computer-based video analysis

The correlation coefficient for the association between QoM and bimanual performance (AHA) was -0.39 ( $p = 0.107$ ) (**table 4**). Manual capacity (B&B) in the affected hand was low to moderate, negatively correlated with QoM in both hands, while there was no correlation between manual capacity (B&B) in the non-affected hand and QoM in any of the hands (**table 4**).

**Table 4:** Correlations between hand function and mirror movements measured using the computer-based video analysis method (QoM). Shaded areas represent statistical significant correlations.

	QoM affected		QoM non-affected	
	Pearson	p-value	Pearson	p-value
<b>AHA (n = 18)</b>	-0.39	0.107	-0.36	0.138
<b>B&amp;B affected (n = 17)</b>	-0.50	0.043	-0.49	0.046
<b>B&amp;B non-affected (n = 17)</b>	-0.25	0.338	-0.13	0.617

## 6. Discussion

### 6.1 Main findings

In accordance with our primary hypothesis, we found that a higher amount of MM in both the affected and the non-affected hand, assessed according to W&T, correlated with poorer bimanual performance, and poorer manual capacity in both hands.

In contrast, we were not able to confirm our secondary hypothesis: That MM assessed in QoM, by our newly developed computer-based method, would show a similar correlation with hand function, as MM assessed according to W&T.

### 6.2 Validity of the results

Chance is unlikely to explain the negative correlations between hand function (bimanual performance and capacity) and MM, as indicated by the low p-values. The study sample was on the other hand low, and lack of statistically significant findings must therefore be interpreted with caution. The latter applies for the low to moderate correlations between QoM and bimanual performance, where a large sample size could have resulted in statistically significant findings. None the less, it is unlikely that this potential type II error explains our inability to confirm our secondary hypothesis.

Mirror movements according to W&T, were scored independently by two observers who were unaware of the results from the two hand function tests (AHA and B&B), while QoM was calculated by the computer. It is thus unlikely that the main results can be explained by observational bias.

Unexpectedly, we discovered significant differences in the two study populations. The children recruited in Trondheim and in Melbourne, showed marked differences on a number of variables. The main differences between the two populations were that the children in Melbourne showed less variability in their amount of MM (W&T), were significantly younger and had significantly poorer hand function than the children in Trondheim. Moreover, the video-recordings in Melbourne were not obtained in

accordance with the instructions, and the bimanual performance was scored using different versions of the AHA. To avoid various problems with bias and confounding factors, resulting from merging the data from the two populations, we decided to exclude the results from the participants in Melbourne completely. The findings of the present study, therefore applies for older children and adolescents with USCP. For completeness, we have included the results obtained in the population from Melbourne in the appendix. The main finding in the latter population, is a much lower, if any correlation between hand function and MM (**appendix**). This lack of correlation is most likely explained by the lack of variability of the MM (W&T) scores. Among the 18 participants in Melbourne, approximately two out of three children had W&T scores of 2; twelve (67 %) in the affected hand, and eleven (61%) in the non-affected hand (**table A2**). We therefore conclude that the selection of children with very little variation in their amount of MM, probably is the principal explanation for the lack of correlation between MM and hand function among the participants from Melbourne. In contrast, we consider the population from Trondheim to be more representative of the whole spectrum of MM in children with USCP, and the remaining part of the discussion will therefore focus on the findings in this population.

### 6.3 Comparison with literature

#### 6.3.1 Hand function and MM assessed qualitatively

Several research groups have investigated whether there is a relationship between hand function and MM scored according to W&T. Varying, however, is how the different studies have chosen to assess hand function. Klingels et al. measured bimanual performance using the AHA, and manual capacity using both the Melbourne Assessment and the Jebsen-Taylor test (42). Consistent with our findings, this group found that that MM in the non-affected hand, correlated negatively with bimanual performance and bimanual capacity in both hands. However, in contrast to our study, they did not find a correlation between MM in the affected hand and any of the measures for hand function (42). Nonetheless, we consider the overall results obtained by Klingels et al. to be consistent with our findings.



Even more similar to our study, Holmstrøm et al. measured bimanual performance using the AHA, and manual capacity using the B&B (38). This research group also found a negative correlation between MM in the non-affected hand and bimanual performance. In contrast to our study, Holmefur et al. did not find an association between MM in the affected hand and bimanual performance, or between MM and manual capacity (38).

A third group (45) also assessed MM according to W&T. This group found that MM affected bimanual performance negatively. Although there were some differences in the design and study population between the study by Adler et al. and our study, the main results were consistent with ours (45).

Thus, studies so far, including our own, point towards a negative correlation between hand function and MM. The results are however conflicting regarding whether it is MM in the non-affected hand, or MM in the affected hand that affect hand function the most, or whether MM affect the affected or the non-affected hand the most. Results are also inconsistent regarding whether MM affect bimanual performance more or less than manual capacity, though most studies point towards MM affecting bimanual performance the most.

### **6.3.2 Hand function and methods aiming to quantify MM**

The newly developed computer-based method aimed to assess MM quantitatively in QoM. Other studies have also used methods intended to quantify MM. Kuhtz-Buschbeck et al. performed in 2000 a study, where they assessed MM quantitatively using a gripping device (34). These authors found, in accordance with our results, that MM affected bimanual performance. They did not find the same association between MM and manual capacity as we did. Manual capacity and bimanual performance were, however, assessed without standardized tests. Moreover, it is possible that the gripping device is extremely sensitive to small contractions; thereby being more sensitive to unspecific movements, and like QoM may not reflect true MM. Also Islam et al. (46) quantified MM with a gripping device. However, these authors did not study bimanual performance or manual capacity but bimanual coordination assessed as fingertip force, using a grip-device. Somewhat inconsistent with our results, these authors did not find that MM (quantified) affected bimanual coordination. Islam et al. could however not completely rule out the

possibility that strong MM may influence the coordination of bimanual tasks, as a substantial part of the group with CP failed to accomplish the task (46). Thus, the studies trying to assess MM quantitatively, including our own study, are even more inconsistent than studies assessing MM qualitatively.

#### 6.4 Interpretation

In this study, MM assessed as QoM were less clearly associated with hand function than MM assessed according to W&T. In another study (unpublished work by Neergård) we found good correlation between the qualitative (W&T) and the quantitative (QoM) measure of MM. We therefore expected to find a similar correlation between QoM and hand function, as between MM assessed according to W&T and hand function. The most likely explanation why we did not find similar correlations could be due to the fact that the computer-based method strictly spoken only describes the amount of movements, and not the quality of the movements, whereas W&T emphasizes the quality of the movements, i.e. that the involuntary movements in the passive hand indeed mimics the intentional movements in the other hand. The computer-based method, and W&T, both scores MM based on visual observations. The computer-based method quantifies the movement in the picture objectively, and will thus not be able to distinguish brief repetitive movements, such as twitching in a finger, as MM. Woods and Teuber is in contrast scored by a clinical observer capable of recognising the quality of the movements. For instance may brief but unsustained repetitive movements be given a score of two according to W&T, while the same brief movements probably would have been given a very low QoM score by the computer. A further limitation of the computer-based method is its sensitivity to disturbances during the video recording; including other movements by the child, shadows and light, and deviations in video camera setup (unpublished work by Neergård).

Mirror movements were not correlated with manual capacity (B&B) in the non-affected hand. This was not surprising, as the capacity of the non-affected hand is unlikely to be affected by MM to the same degree as the affected hand. Mirror movements are mainly triggered in the non-affected hand when the affected hand is performing intentional movements (38). In children with USCP, one of the brain hemispheres has a lesion. A

high degree of MM in the non-affected hand is associated with persistent ipsilateral projection from the non-damaged hemisphere to the affected hand (38). When the same hemisphere controls both limbs, intentional movements in the affected limb through ipsilateral projections from the healthy hemisphere, might trigger MM in the non-affected hand.

A potential biological explanation of the negative association between MM and bimanual performance and manual capacity may be related to the fact that the amount of MM may indicate differences in the organization of the cortico-spinal motor tracts, which in turn may affect the effectiveness of interventions (38). Because of its symmetrical nature, MM will affect bimanual activities where asymmetrical hand skills are needed. Kuhtz-Buschbeck et al. found that motor commands to the affected hand, in particular influenced the actions of the non-affected hand. They also observed that some patients did not assist with their affected hand in bimanual tasks, and speculated whether this could be a strategy to avoid interference from the affected to the non-affected hand (34).

The findings that MM adversely affect bimanual performance and manual capacity may also have consequences for intervention, as suggested by Kuhtz-Buschbeck (34). In their study, Kuhtz-Buschbeck et al. proposed that therapeutic strategies based on constraining the non-affected hand could be wrong for those with strong MM. Instead therapeutic strategies should be bimanual for these children (34). In a recent conference abstract by Adler et al. (50), an intensive therapeutic regimen for children with USCP with strictly bimanual therapy, is described to show improvements in unimanual capacity as well as bimanual performance. The group concludes that the subjects improve by learning to control their MM voluntarily. Surprisingly, however, no change could be seen in MM assessed according to W&T, or in MM measured using a gripping device (50).

## 6.5 Conclusion

There is a moderate to high negative correlation between MM and bimanual performance and capacity in both hands, among children and adolescents with USCP over the age of 10. The correlation between our recently developed quantitative method

to assess MM, and hand function was lower – with this method, only the negative correlation between hand capacity and MM reached statistical significance.

## 7. Appendix

Displaying the differences in results between the two study populations, from Trondheim and Melbourne respectively.

### 7.2 Hand function

The children from Melbourne scored considerably lower both in the AHA test and in the B&B test, than the children from Trondheim (**table A1**). The children from Melbourne also had a marked lower variance both in AHA scores and B&B scores than the participants from Trondheim (**figure A1**).

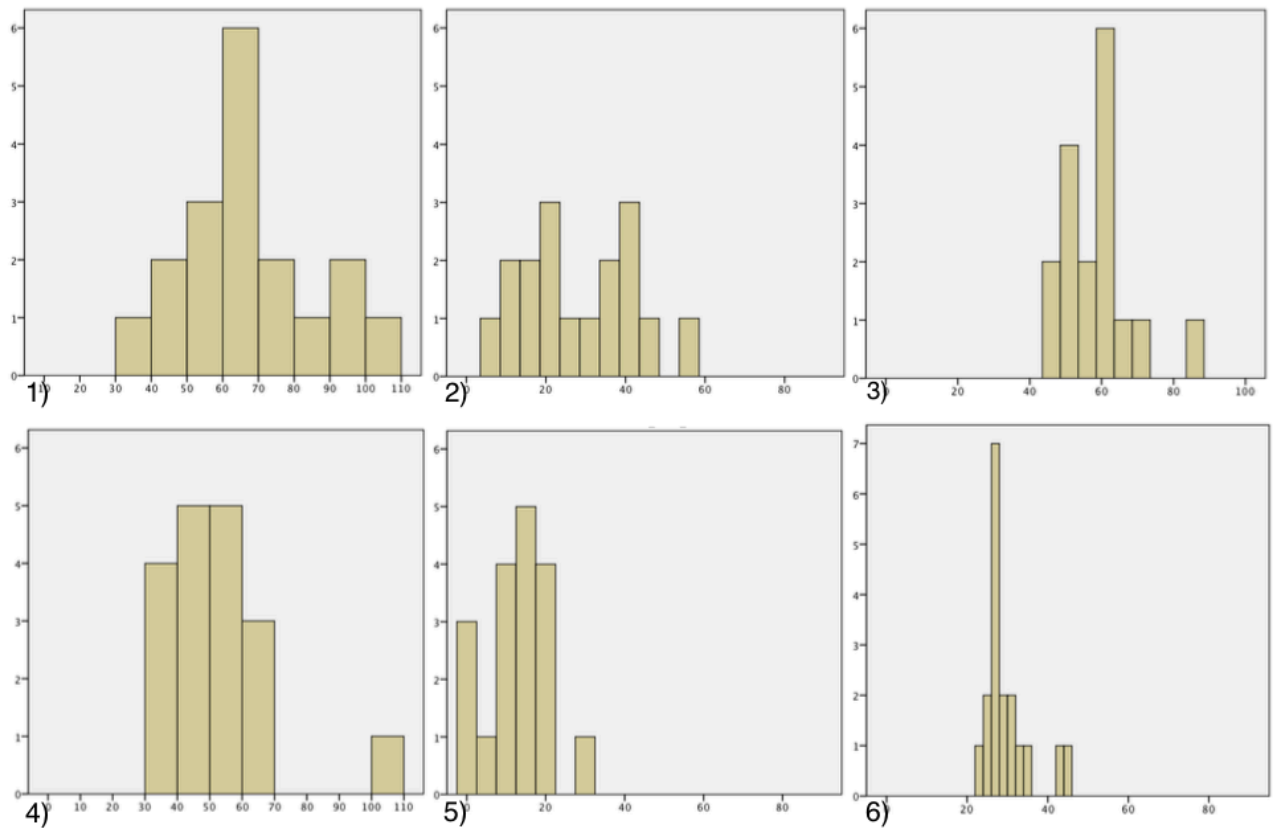
**Table A1:** Hand function measured using the Box and Block test (B&B), and the Assisting Hand Assessment (AHA), among children with unilateral spastic cerebral palsy.

	<b>Norway</b>	<b>Australia</b>	
<b>AHA</b>	n = 18	n = 18	
	mean (std)	66.2 (16.8)	50 (16.3)
	range	37-100	30-100
<b>B&amp;B affected</b>	n = 17	n = 18	
	mean (std)	28.4 (14.2)	12.7 (7.9)
	range	6-55	0-32
<b>B&amp;B non-affected</b>	n = 17	n = 18	
	mean (std)	59.2 (9.9)	29.5 (5.8)
	range	46-87	23-44

**Figure A1:** Distribution of the Assisting hand Assessment (AHA) scores, and the Box and Block (B&B) scores.

Top: Trondheim: 1) AHA, 2) B&B affected hand, 3) B&B non-affected hand.

Bottom: Melbourne: 4) AHA, 5) B&B affected hand, 6) B&B non-affected hand.



## 7.3 Mirror movements

### 7.3.1 Mirror movements – Woods and Teuber

The distribution of W&T scores is shown in **table A2**. The median W&T scores are shown in **table A3**. The participants from Melbourne had more MM (W&T 2-4) than the participants from Trondheim (**table A2-A3**). The participants from Melbourne had more MM in the non-affected hand, than in the affected hand ( $p = 0.0083$ ) (**table A2-A3**). The participants from Melbourne also had a considerably lower spread in W&T scores than the participants from Trondheim, mainly due to a higher proportion of children with a W&T score of 2 among the participants from Melbourne (**table A2**).

**Table A2:** Distribution of Woods and Teuber scores.

	W&T scores	Trondheim	Melbourne
<b>Affected side</b>	0	4 (22 %)	1 (6 %)
	1	6 (33 %)	4 (22 %)
	2	3 (17 %)	12 (67 %)
	3	2 (11 %)	1 (6 %)
	4	3 (17 %)	0
	0-1	10 (55 %)	5 (30%)
	2-4	8 (45 %)	13 (70%)
<b>Non-affected side</b>	0	6 (33 %)	1 (6 %)
	1	3 (17 %)	2 (11 %)
	2	6 (33 %)	11 (61 %)
	3	1 (6 %)	3 (17 %)
	4	2 (11 %)	1 (6 %)
	0-1	9 (50 %)	3 (17 %)
	2-4	9 (50 %)	14 (83 %)

### 7.3.2 Mirror movements – Computer-based video analysis (QoM)

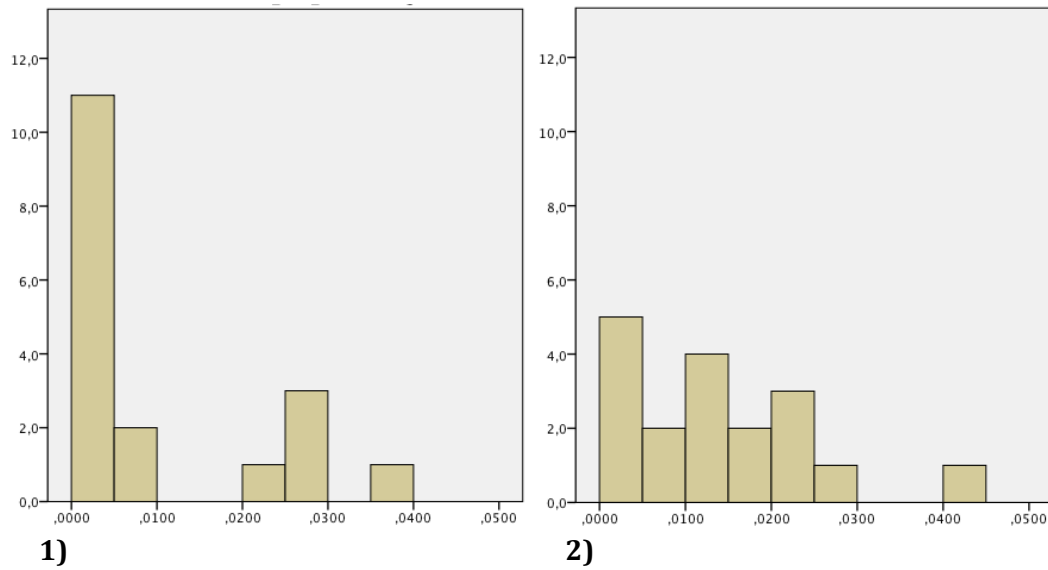
The children from Melbourne had higher mean QoM values than the participants from Trondheim (**table A3**). The Quantity of Motion scores belonging to the participants from Melbourne had a wider distribution than the scores belonging to the participants from Trondheim (**figure A1-A2**). The participants from Melbourne had more MM in the non-affected hand, than in the affected hand ( $p = 0.245$ ), while the participants in Trondheim had more MM in the affected hand, than in the non-affected hand ( $p = 0.129$ ).

**Table A3:** Table showing average values of mirror movements scored with Woods and Teuber and Quantity of Motion respectively.

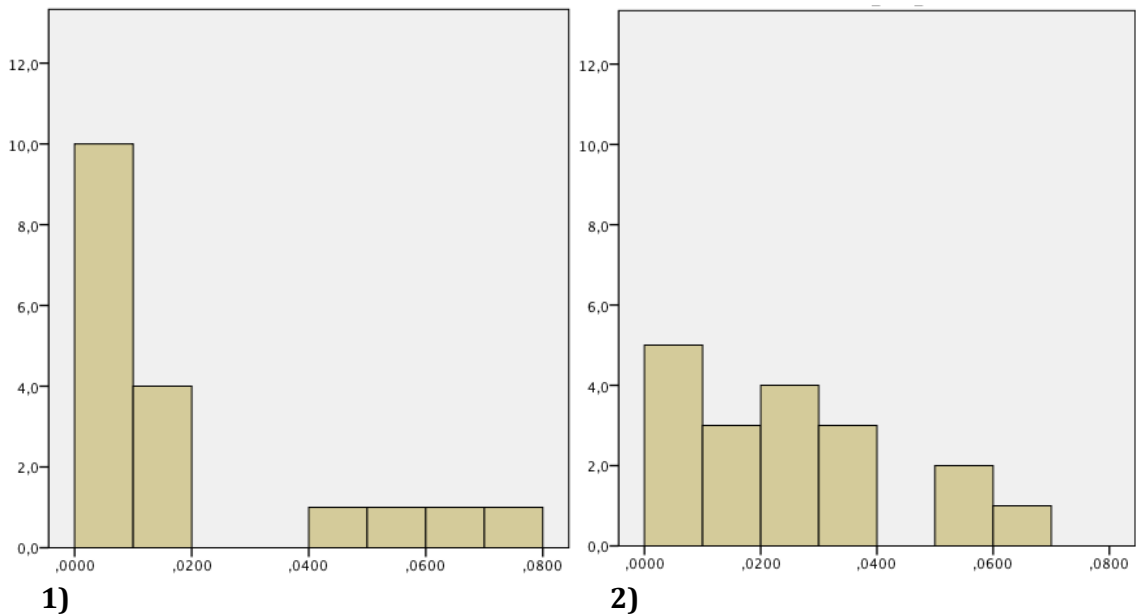
			<b>Affected hand</b>	<b>Non-affected hand</b>
<b>Trondheim</b>	<b>W&amp;T (n = 18)</b>	median (IQR)	1 (0.75-3)	1.5 (0-2)
	<b>QoM (n=18)</b>	mean (SD)	0.010 (0.013)	0.007 (0.010)
<b>Melbourne</b>	<b>W&amp;T (n = 18)</b>	median (IQR)	2 (1-2)	2 (2-2.5)
	<b>QoM (n=18)</b>	mean (SD)	0.014 (0.011)	0.016 (0.013)



**Figure A2:** Displaying the frequency (y-axis) of QoM affected hand (x-axis). Participants from: 1) Trondheim, 2) Australia.



**Figure A3:** Displaying the frequency (y-axis) of QoM non-affected hand (x-axis). Participants from: 1) Trondheim, 2) Australia



#### 7.4 Correlation between hand function and MM

In contrast to the group from Trondheim, no correlation could be found between hand function and MM among the participants from Melbourne (**table A4-A5**)

**Table A4:** Correlations between hand function and mirror movements assessed according to Woods and Teuber (W&T). Shaded areas represent statistical significant correlations.

	Trondheim				Melbourne			
	W&T affected		W&T non-affected		W&T affected		W&T non-affected	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
<b>AHA</b> (n = 18)	-0.65	0.004	-0.50	0.034	0.16	0.527	0.07	0.787
<b>B&amp;B affected</b> (n = 17)	-0.66	0.004	-0.59	0.013	0.03	0.899	-0.01	0.974
<b>B&amp;B non-affected</b> (n = 17)	-0.10	0.711	-0.15	0.574	-0.06	0.813	0.21	0.395

**Table A5:** Correlations between hand function and mirror movements measured using the computer-based video analysis method (QoM). Shaded areas represent statistical significant correlations.

	Trondheim				Melbourne			
	QoM affected		QoM non-affected		QoM affected		QoM non-affected	
	Pearson	p-value	Pearson	p-value	Pearson	p-value	Pearson	p-value
<b>AHA</b> (n = 18)	-0,39	0,107	-0,36	0,138	0.15	0.565	-0.07	0.770
<b>B&amp;B affected</b> (n = 17)	-0,50	0,043	-0,49	0,046	0.16	0.539	-0.07	0.784
<b>B&amp;B non-affected</b> (n = 17)	-0,25	0,338	-0,13	0,617	-0.08	0.763	0.04	0.877

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