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Cognition and Bimanual Performance in Children with Spastic Unilateral Cerebral Palsy: A population – based study

Master's thesis in Activity and Movement
Supervisor: Ann-Kristin Elvrum
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Thesis submitted for the master´s degree in Activity and Movement

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Abstract

Background: Children with unilateral cerebral palsy (CP) may experience difficulties in performing daily activities, due to reduced bimanual performance and cognitive impairments. Both reduced bimanual performance and cognitive impairments may interact and hamper the acquisition of functional skills in daily life. Therefore, it is important to gain further insight into the interplay between cognition and bimanual performance in children with unilateral CP.
Aim: *Primary aim*: examine the association and relationship between hand function and cognition in a population-based sample of children with spastic unilateral CP. *Secondary aim*: to explore the strength of the associations between bimanual performance and cognitive functions. **Method:** A cross-sectional study design was used, and registered data from Cerebral Palsy Register of Norway (CPRN), formal follow-up protocol for cognition (CP*Cog)* and Cerebral Palsy Follow-up Program (CPOP) was used in this study. Pearson *r* was used to examine correlation between the variable, and a linear multiple linear regression analysis was used to analyse the relationship between the variables.

Results: 83 children were included in the final sample mean. There was a moderate correlation between full-scale IQ and bimanual performance, but full-scale IQ did not significantly contribute to the variance in bimanual performance (AHA). However, strong correlations were found between bimanual performance, manual ability (MACS) and active use of the affected hand (House). Both manual ability and active use of the affected hand significantly contribute to 65% of the variance in bimanual performance. There were weak correlations between FRI, PSI, WMI and VSI (Wechsler tests) and bimanual performance (AHA), but the indexes did not significantly contribute to the variance in bimanual performance.

Discussion: Manual ability and active use of the affected hand have an effect on bimanual performance, nevertheless, IQ does not. It is possible that other cognitive components, such as executive function, can have an effect on bimanual performance. Therefore, future research should consider examining the relationship between executive function and bimanual performance in children with unilateral CP.

Keywords: Unilateral Cerebral Palsy, Hemiplegic, Children, Bimanual Performance, IQ, Cognition, Hand Function, Assisting Hand Assessment.

Introduction

Cerebral Palsy (CP) is the most common cause of physical disability in children and youth worldwide with a reported prevalence between 1.5 and 3 per 1000 in various populations (1). Children with CP are described as the most prominent group within children´s rehabilitation (2). Cerebral palsy is an umbrella term of a wide range of neurodevelopmental conditions which leads to a variety of motor disabilities. These motor disabilities are caused by brain injury in the immature brain that occurs either in the prenatal period, perinatal period, or in the neonatal period and up to two years of age (1, 3). The brain injury that has occurred is static, but manifestations in motor functioning can vary depending on the size and localization of the damage and can further change over time. Although CP is primarily a movement disorder, it can also affect other functions of the central nervous system. In addition to epilepsy, impairments to cognition, perception, vision, hearing, and communication have all been observed (3). The condition is categorized based on dominant motor pattern into the following subtypes: spastic, dyskinetic, and atactic CP. Among which spastic CP is the most common, affecting approximately 80 – 90% of all children with CP of varying severity (4-6). Depending on which body parts that are affected and what kind of motor signs the child is showing, children with spastic CP are further classified within spastic unilateral (hemiplegia) or spastic bilateral (diplegia and quadriplegia) CP (7).

Children with unilateral CP may experience difficulties in performing meaningful daily activities as a result of the motor impairments, which affects one side of the body (8). The most prominent motor features on the affected side are impaired motor control and coordination, increased muscle tone (spasticity), reduced tempo and grip strength, and reduced range of motion (9, 10). Normally, typically developed children progress and acquire motor, cognitive, emotional and social skills as well as abilities through numerous developmental milestones throughout infancy and childhood (11). The development of independence in activities of daily living is influenced by contextual variables such as family environment and culture, along with improving their gross motor capacity, and manual, intellectual, and communicative functions (12). This type of independence is commonly fully developed around seven years of age in typically developing children (13). However, for children with unilateral CP, as a consequence of having motor disabilities, acquiring independence in daily activities can be challenging (13).

One of the strongest predictors of restricted participation in daily activities is having limited ability to handle and manipulate objects (10). For children with unilateral CP it is natural and functional to use their efficient hand while participating in daily activities that only demand the use of one hand (9). This may be due to their limited resources to reach, hold, manipulate and release objects with their affected hand (14). Still, most of our daily activities, such as self-care-, school, -social – and leisure activities demand the use of both hands (9).

Various classifications and outcome measures can be used to describe how children with unilateral CP handle objects in daily life. Two versions of such a classification system are Manual Ability Classification System (MACS) and the Mini-Manual Ability Classification System that classify how children with unilateral CP handles objects in daily activities (15, 16). The MACS and the Mini-MACS are suitable for children aged 1 – 4 years and from 4 years and older, respectively. Both versions of the classification system consist of a five-level classification system where each level describes how the child is using their hands and handling objects in bimanual activities. Children on level I in both MACS and Mini-MACS handles objects easily in everyday activities, whereas children on level V do not handle objects and need assistance when handling objects in daily activities (15). Normally, most children with unilateral CP classify within level I-III on MACS and Mini-MACS (5, 17).

However, classifications only describe hand function in groups of children according to common characteristics. In addition to classification systems, it is therefore necessary to use standardized outcome measures to be able to describe hand function in more detail (18). Assisting Hand Assessment (AHA) is a standardized and criteria-based assessment -tool developed for children with unilateral CP between the ages of 18 months to 18 years (18). AHA measures and describes how effectively the child uses their affected hand spontaneously in activities that require bimanual hand use in a natural environment (19).

In children with unilateral CP the functional use of the affected hand can vary from no functional ability to good ability to manipulate and handle objects (10). Thus, it is useful to gain knowledge regarding the functional use of each hand specifically. The House Functional Classification System (House) was developed for children with CP aged 2-20 years and classifies hand function in each hand separately. The assessment-tool describes the role of the assessed hand in children with CP as a passive or active assist in bimanual activities (20, 21).

Children with CP often participate in less varying and more passive recreational activities compared to typically developed children (22). There is a broad agreement that this is largely due to their motor impairments (13). The motor impairments are either caused by antenatal or perinatal insult to the immature brain (8). Disturbed cerebral control of motor function is largely related to corticospinal tract damage, the corticospinal tract being the major descending tract that controls skilled, fractioned and voluntary hand movements (9).

Previous research has reported a correlation between both reduced hand function and gross motor function with limited independence in daily activities in children with unilateral CP (13, 23). One study in particular, which investigated self-care and mobility skill related to manual abilities and gross motor functions in children with CP, found a strong relationship between functional skills in self-care and MACS classification levels (13). In other words; children with higher functioning levels in MACS are more capable in self-care activities than children with lower functioning levels. In addition, the results indicated that functional skills were found to increase with age in children who classified at MACS levels I and II. However, little or no association with age was found in children at other classification levels (13). These findings are similar to the findings in the study by Smits, et al. (23) study, which examined the course of capabilities in self-care, mobility and social function in school-aged children with CP. The results of this study also indicated that hand function is strongly correlated with everyday functioning (23).

Limitations children with spastic unilateral CP experience in daily activities have led to a variety of evidence-based interventions to enhance the children´s functions (24). Today, most of the interventions that are being used have a “top-down” approach which emphasizes the importance of functional skills and practice through purposeful activities in the children’s natural environment (25). Some of these interventions targeting upper-limb function are “Constraint-Induced Movement Therapy” (CIMT) and bimanual therapy (26). These interventions have proven to be effective for children with unilateral CP, however, other studies indicate that not children with unilateral CP respond to these interventions (24). Several factors can influence why some of these children do not benefit from CIMT and bimanually therapy, but because skilled task performance involves several cognitive processes, it is reasonable to believe that cognition can influence effective bimanual performance in everyday activities (24).

Cognition is defined as *"the mental actions or processes of acquiring knowledge and understanding through thought, experience, and the senses"* (24), and there are several studies that explain a possible relationship between motor and cognitive skills in children (27). Some of these studies have shown interactions between the prefrontal cortex, the cerebellum, and the basal ganglia during several motor and cognitive tasks, especially when the task is new or difficult, if the conditions in the context of a task changes, or when concentration is needed to perform the task (28, 29). Some studies have also shown that early in the learning process, cognitive processes, such as working memory and error detection can play a key role in motor skill learning (30). Additionally, research has shown that motor and cognitive skills have several common underlying processes, for instance sequencing, monitoring, and planning (31).

Cerebral lesions associated with CP represent a biological constraint affecting the typical developmental trajectory of different cognitive functions and can entail intellectual disability (ID) as well as specific cognitive impairments (32) . Children with unilateral spastic CP are at risk of developing a wide range of cognitive impairments due to the nature of the underlying lesions (32). The brain injuries in children with unilateral CP are commonly grouped into broad categories, where around 50% of the children are observed to have periventricular white matter lesions (PWM), and around 20% are observed to have cortical/subcortical grey matter lesions (GM) (33). PWM can cause secondary changes to connected grey matter structures and extend to cortical regions (8). Grey matter lesions may impact critical structures of the brain, such as the basal ganglia, thalamus and cortical grey matter, which can lead to more severe impairments of several functions, in particular motor function, attention and executive function (8, 33). In addition, studies have reported both that general cognitive functioning (IQ) is one of the strongest predictors of psychiatric problems in children with unilateral CP (34).

There is a broad variation in cognitive function in children with CP (35). Most children with spastic unilateral CP have a normal cognition where around 81-90% are reported to have an IQ higher than 70 (36). However, children with unilateral CP may experience cognitive impairments such as reduced executive functions and problems related to visual-spatial reasoning and adaptive functioning (24, 35). Of special interest is visual-spatial perception and reasoning, as this is related to how children perceive and problem-solve tasks requiring the integration of visual stimuli and fine-motor performance. In children with unilateral CP, this has found to be more affected than verbal cognition, regardless of lesion side (36-38). Thus, both cognitive impairments and reduced hand function may interact and hamper the acquisition of functional skills in daily life. It is therefore important to gain further insight into the interplay between hand function and cognition in children with unilateral CP. In children it is common to measure cognition using intelligence tests. The most commonly used tests of intelligence in Norway are the Wechsler tests (39). These tests provide a measure of IQ, as well as measures of verbal cognition, visual-spatial perception, visual-spatial reasoning (also referred to as fluid reasoning), attention (memory span and working memory) and processing speed (40, 41).

Aim of the study

The primary aim of this current study is to examine the relationship between bimanual performance, manual ability, functional use of the involved hand and cognition in a population - based sample of children with spastic unilateral CP. We hypothesize that we will find a strong relationship between bimanual performance and cognition (i.e. Full-Scale IQ). The secondary aim is to explore the strength of the associations between bimanual performance and cognitive functions such as verbal cognition, visual-spatial perception, visual-spatial reasoning, attention and processing speed.

Methodology
Study design
This is a population-based correlation study using a descriptive cross-sectional design to describe the relationship between hand function and cognition in children with spastic unilateral cerebral palsy. Cross-sectional studies are some of the most common and well-known study designs and are used to describe and compare characteristics that exist in a population (42, 43). This study design is not used to determine cause – and – effect on relationships between different variables, but rather to investigate possible associations between them (43). Cross-sectional studies take place at a short or single point in time and do not involve manipulating variables. They also allow researchers to look at numerous characteristics at once, and are often used to look at the prevalence of a particular outcome of interest for the population or a subgroup thereof (43).

Participants
Eligible participants for inclusion in this study were children included in the Cerebral Palsy Register of Norway (CPRN) diagnosed with unilateral CP and born between 2004-2013 (Aged 5-15 years). CPRN is a nationwide register collecting health related information of children with CP at the age of diagnosis, at five years of age and between 13-15 years of age. Included in CPRN is a formal follow-up protocol for cognition, CP*Cog*. In addition, data from the national Cerebral Palsy Follow-Up Program (CPOP) is linked to CPRN. Both CPRN and CPOP monitor children with CP in Norway, and CPRN is estimated to include 90% of the total CP population. In this study, we used available data from CPRN and CPOP describing hand function and cognition registered at five-year follow-up for children with spastic unilateral CP. We wanted to use data describing participants general level of cognition assessed with a Wechsler test, as well as their executive functions assessed with Behaviour Rating Inventory of Executive Function (BRIEF). However, there were not enough data on BRIEF to be included in the final analysis. To be included in the final analysis, children with spastic unilateral CP had to have bimanual performance assessed with Assisting Hand Assessment, functional use of the involved hand registered with the House Functional Classification System, and a registered formal cognition assessment. A total of 592 children with spastic unilateral CP were enrolled in the data collection from CPRN and CPOP. Of these, data from 83 children were included in the final analysis. A study flow chart showing the inclusion-process for the included participants in the statistical analysis can be found in appendix 1.

Ethical considerations

All parents to the participants in this study provided written informed consent when their child was included in the CPRN register and in the CPOP follow-up program. In addition, the current study was approved by the Regional Committee for Medical and Health Research Ethics of Mid-Norway (REK 94904), and CPRN and CPOP permitted the use of registered data in this study using de-identified data with an ID code for each participant.

Hand function

Assessments of hand function, detailed below, were administered and scored by licenced therapists and physicians at the habilitation services in Norway.

Classification of Manual Abilities

Hand function was classified using the Manual Ability Classification System. As mentioned previous MACS is used to classify how children aged 1-4 and 4-18 years use both hands when handling objects in everyday activities (15). The psychometric properties of the MACS and Mini-MACS have been assessed with analysis of content, criterion, construct validity, and reliability (15, 16, 44, 45).

Assisting Hand Assessment

Bimanual performance was measured using the Assisting Hand Assessment (AHA) and will be used as a dependent variable in this study. As mentioned previously, the AHA is used to assess bimanual performance in children aged 18 months to 18 years. The AHA has specific age-related test kits comprised of standardized toys requiring the use of both hands. The evaluation is administered in two steps; First, a semi-structured video-recorded play session is conducted. Second, the therapist uses the videotape to score the child´s bimanual performance to 20 items scored on a four-point rating scale (18, 46). The AHA was developed by the use of Rasch measurement analysis, and the raw score, ranging from 20-80, is therefore converted into an interval level logits-based AHA-unit ranging from 0 to 100 (18, 46). The AHA has been found to be valid and reliable with evidence of content and construct validity, interrater and intrarater reliability and test-retest reliability (18, 19, 47-49).

House Functional Classification

Classification of hand function in each hand separately was registered using the House Functional Classification (House). This classification-tool uses a nine-point scale that ranges from a score of zero, meaning the child does not use the hand, to a score of eight, meaning the child performs active spontaneous use of the hand (20). The House is an observational tool and includes a manual, which can be completed by the patient, parents, therapists, or a physician (20). A modified version of the original House Functional Classification has been developed, and both versions are reported to be reliable and valid tools (50, 51).

Cognition

As part of the follow-up of children with CP in Norway, a protocol for follow-up of cognition, the CP*Cog*, was developed. This recommends an assessment of cognition at 5 to 6 and 12 to 13 years of age and the Wechsler tests are some of the instruments recommended for the assessment (52).

Wechsler tests

The Wechsler tests are used to measure intellectual ability and are available in different versions suitable for separate age groups. For children aged 2:6 to 7:7 years of age, the Wechsler Preschool and Primary Scale of Intelligence is used (WPPSI-IV) (40), while the Wechsler Intelligence Scale for Children (WISC-V) is normed for children aged 6:0-16:11 years of age(41). The intelligence tests are developed to provide an overall measure of general cognitive ability and measure intellectual functioning in children and youth (40, 41). The tests give an overall measure of intellectual functioning by providing a full-scale IQ score, as well as the five index scores: Verbal Comprehension Index (VCI), Visual Spatial Index (VSI), Fluid Reasoning Index (FRI), Working Memory Index (WMI) and Processing Speed Index (PSI). The tests are reported as both valid and reliable (40, 41).

The psychologists entering the test results into CPRN, enter the sum of scaled scores for the five indexes, and not in the index scores. This was done deliberately, to ensure that there should always be a psychologist present when interpreting the cognitive data from the CPRN and to safeguard against an IQ- score below 70 automatically being interpreted as evidence of an intellectual disability. Additionally, when entering the sum of scaled scores, the psychologists should also enter any diagnosis of cognitive functioning assigned to the child. In order to analyse data of cognition, the sum of scaled scores from WPPSI-IV and WISC-V were transformed, by a licensed neuropsychologist, to standardized scores for all five indexes as well as for the full-scale IQ (FSIQ). Index scores are derived from the sum of two scaled scores. However, in some instances only the scaled scores from one subtest was available, and/or the sum of scaled scores (see table 1 for an overview over available cognitive data). An index score was only calculated if 1) scaled scores from both subtests were available, 2) one index score and the sum of two scaled scores were available, or 3) the sum of scaled scores were available.

The FSIQ in WPPSI-IV is based on six subtests, and for 59 of 93 participants the scaled scores from all six subtests were available. For the remaining participants, the sum of four (N=19) and five (N=14) subtests were used to estimate the sum of six scaled scores, in accordance with the specifications in the manual (40). For WISC-V, the FSIQ is based on the result of seven subtests for 22 participants and an estimation of sum of seven scaled scores for 31 participants who had completed six subtests, in accordance with the specifications in the manual (41). For four participants who had completed four or five subtests, the mean scores were used to estimate what the sum of seven scaled scores would be.

Some children were assessed with previous versions of the WPPSI or the WISC, where the indexes were not exactly similar to the indexes in the newest version. For these children, only the indexes that are the most similar, i.e., the verbal comprehension, working memory and processing speed indexes, were utilized, as well as the FSIQ. In the newest version of the WPPSI and WISC, the five indexes are similar. The results from children assessed with WPPSI and WISC were therefore combined; and Wechsler, VCI, VSI, FRI, WMI and PSI were computed. Only one child had results from both WPPSI and WISC. For that child the scores from the WPPSI were chosen, as they were the most complete.

Table 1. Number of children with scores from subtests and number of children for whom indexes were derived.

Index	Subtests	WPPSI	WISC	Wechsler
Verbal comprehension index (VCI)		87	61	148
	Similarities (WPPSI/WISC)	72	56	
	Information (WPPSI)	91		
	Vocabulary (WISC)		58	
Visual spatial index (VSI)		71	25	96
	Block Design (WPPSI/WISC)	91	56	
	Object Assembly (WPPSI)	67		

	Visual Puzzles (WISC)		24	
Fluid reasoning index (FRI)		77	25	102
	Matrix Reasoning (WPPSI/WISC)	90	56	
	Picture Concepts (WPPSI)	74		
	Figure Weights (WISC)		23	
Working memory index (WMI)		52	49	101
	Picture Span (WPPSI/WISC)	71	23	
	Zoo Locations (WPPSI)	48		
	Digit Span (WISC)		57	
Processing speed index (PSI)		66	60	126
	Bug/Symbol Search (WPPSI/WISC)	79	55	
	Cancellation (WPPSI)	53		
	Coding (WISC)		55	
Full-scale IQ (FSIQ)		92	58	149[1]

[1]One child had FSIQ from both WPPSI and WISC

Statistical analysis

The data from CPRN and CPOP were transferred to and analysed with IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, N.Y., USA). Interval level were described through means, standard deviation, minimum and maximum. Nominal and ordinal data were described through their frequency. Through visual inspection, all variables seemed to be normally distributed, however, Shapiro-Wilk testing of normality indicated that the FSIQ was not normally distributed. Investigating the boxplots, we identified one “outlier” with an IQ of 129 in the FSIQ variable. When this participant was excluded the FSIQ was found to be normally distributed according to Shapiro-Wilk testing. Therefore, we concluded that the FSIQ was essentially normally distributed and parametric statistics could be used. To examine correlations between the variables, the Pearson correlation *r* was used. Linear regression was performed to examine the strengths and explanatory power of the variables House, MACS and IQ on the AHA unit. Scatterplots and boxplots were chosen to illustrate results presenting associations between variables and their strengths and directions. Because 98% of the children scored 7 or 8 on the House Functional Classification on their non-affected hand, we did not include this variable in the analysis. Therefore, we used the variable that describes the active use of the affected hand from House when performing correlation – and linear regression analysis.

Linear regression modelled the relationship between bimanual performance and cognition. A simultaneous method was used with nine variables. These included two measures of hand function (House and MACS), five cognitive index scores (VCI, VSI, FRI, WMI, PSI) and two demographic variables (age, sex). Variables that did not contribute significantly to the model were removed. In addition, independence, normality, constant variance of the residuals, and outliers were examined to assess whether the assumptions of linear regression were met. When performing linear regression, exclude cases listwise was used, because we wanted to include participants that had data from all the variables. Significant values were set to $p < 0.05$.

Results

Demographics

A total of 592 children were enrolled in the data collection from CPRN and CPOP.

Table 2: This table show the characteristics of the included and excluded children

Table 2. Characteristics	*Included*	*Excluded*	*Total*
Number of children: n (%)	83 (14)	509 (86)	592 (100)
Age: n	83 (14)	509 (86)	568 (95.9)
Mean (SD)	5 y 5 m (1y)	5 y 8 m (1y 5m)	5y 8m (1y 5m)
Missing System n (%)	-	24 (4.1)	
Diagnosed with spastic unilateral CP: n	83	509 (86)	592 (100)
Left-sided: n (%)	51 (61.4)	218 (42.8)	342 (57.8)
Right-Sided: n (%)	32 (38.6)	291 (57.2)	250 (42.2)
Sex: n	83 (14)	509 (86)	592 (100)
Male: n (%)	49 (59.0)	278 (54.6)	327 (55.2)
Female: n (%)	34 (41.0)	231 (45.4)	265 (44.8)
Severe Visual Impairment: n	83 (14)	509 (86)	459 (77.5)
Yes: n (%)	2 (2.4)	4 (0.80)	6 (1.0)
No: n (%)	79 (95.2)	455 (89.4)	534 (90.2)
Unknown: n (%)	2 (2.4)	50 (9.80)	52 (8.8)
MACS level: n (%)	83 (14)	509 (85.9)	592 (100)
I	29 (34.9)	261 (53.7)	290 (51.0)
II	40 (48.2)	163 (33.5)	203 (35.7)
III	12 (16.9)	56 (11.5)	70 (12.3)
IV	-	6 (1.20)	6 (1.1)
V	-	-	-
Not classified	-	23 (4.50)	23 (3.9)
House level: n (%)	83 (14.0)	430 (84.7)	592 (100)
0 (does not use)	-	3 (0.70)	3 (0.5)
1-3 (stabilizes without grasp or passive grasp)	8 (9.6)	45 (10.5)	53 (9.0)
4-6 (poor to good active grasp)	48 (57.8)	170 (39.5)	218 (36.8)
7-8 (only reduced dexterity or no limitation)	27 (32.5)	212 (49.3)	239 (40.4)
Not classified	-	79 (15.5)	79 (13.3)
Assisting Hand Assessment Unit: n (%)	83 (14.0)	180 (35.4)	263 (44.4)
Mean (SD)	64.2 (18.1)	63.7 (18.6)	63.7 (18.55)
Missing system N (%)	-	329 (64.6)	
Whechsler tests – WISC and WPPSI	83 (55.7)	66 (44.3)	149 (25.1)
Mean (SD)	83.2 (15.91)	84.9 (19.1)	83.59 (17.33)
Missing system N (%)	-	443 (87.0)	
Brain MRI: n (%)	83 (14.0)	509 (86.0)	592 (100)
Normal	3 (3.60)	12 (2.40)	15 (2.5)
White matter injury	24 (28.9)	154 (30.3)	178 (30.1)
Grey matter injury	25 (30.1)	119 (23.4)	144 (24.3)
Congenital malformations	3 (3.60)	19 (3.70)	22 (3.7)
Mixed (White and grey matter)	3 (3.60)	12 (2.40)	15 (2.5)
Mixed (Congenital malformations and grey matter)	-	3 (0.60)	3 (0.5)
Other	1 (1.2)	17 (3.30)	18 (3.0)
Unknown	-	8 (1.60)	8 (1.4)
Missing system N (%)	24 (28.9)	165 (32.4)	189 (31.9)

N=number; CP=cerebral palsy; MACS=Manual Ability Classification System; House= House Functional Classification; WISC= Wechsler Intelligence Scale for Children; WPPSI= Wechsler Preschool and Primary Scale of Intelligence.

Table 2 compares the demographic data for children who were included in the final analyses (n=83) to the excluded children (n=509). There were more males than females both in the included (59%) and the excluded (54.6%) group, and about 90 % of the participants had no severe visual impairment in either group. Regarding assessment of bimanual performance, both groups had similar mean AHA units of 64.2 and 63.7. In the included group, there are more children classified in MACS level II (48.2%) compared to the excluded group (33.5%) and the total population (35.7%). Furthermore, the House classification also indicates some differences between the groups with more children having only reduced dexterity or no limitations in the affected hand in the excluded group (49.3%) compared to the included group (32.5%). In both groups only 10% do not have an active grasp. Regarding cognitive function, both groups have similar IQ-levels measured with the Wechsler tests with mean scores of 83.2 (included group) and 84.9 (excluded group). Furthermore, in both groups, most of the participants had either a white matter injury or a grey matter injury.

Correlations between cognition and hand function

The Pearson *r* correlation analysis was selected to investigate the correlation between bimanual performance (AHA) and the other variables (FSIQ, MACS and House). Table 3 presents the correlations between the variables.

Table 3. Pearson r correlation between variables (n=83)

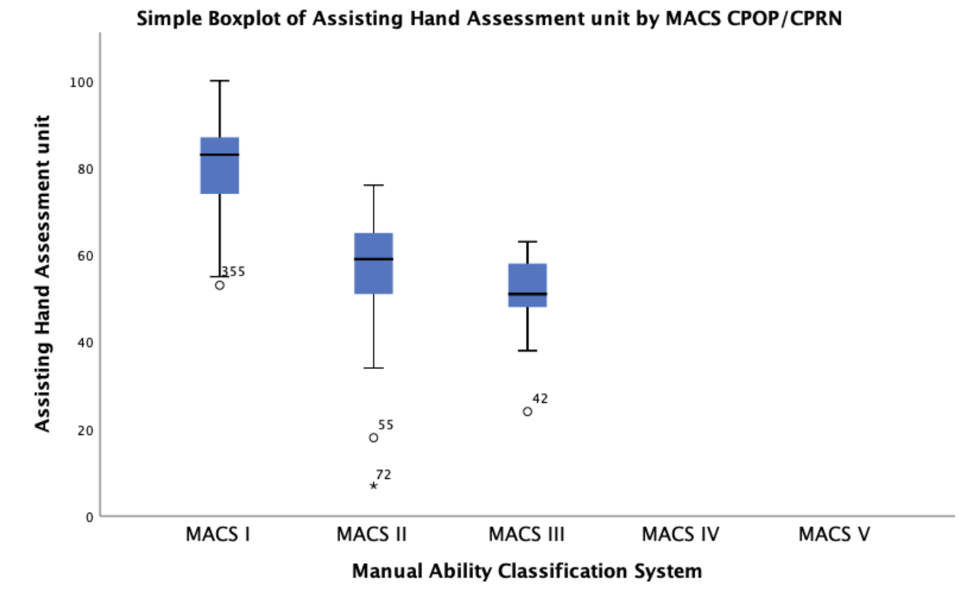
Variables	AHA unit	FSIQ	MACS	House
AHA unit	-			
FSIQ	0.354**	-		
MACS	-0.653**	-0.304**	-	
House	0.805**	0.301**	-0.722**	-

** Correlation is significant at the 0.01 level (2-tailed).
AHA Unit= Assisting Hand Assessment unit; FSIQ= Full-Scale IQ (WPPSI & WISC); MACS=Manual Ability Classification System; House= House Functional Classification.

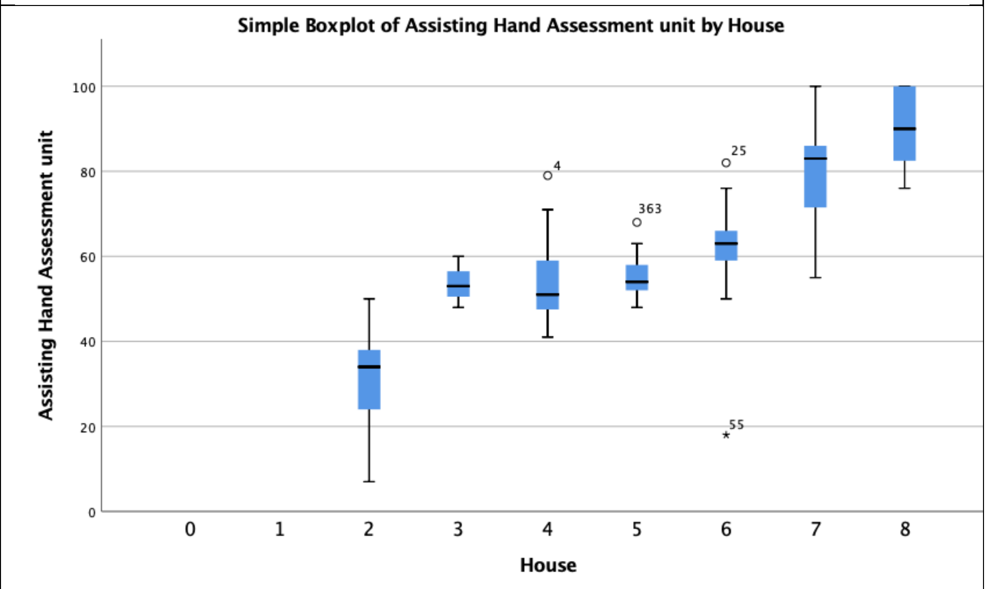
The results show that there are significant correlations between all the variables. There is a strong positive correlation between bimanual performance and active use of the affected hand (House). Furthermore, there is a relatively strong negative correlation between bimanual performance and manual ability classified with MACS. The results also indicate significant, but weaker correlations between cognition and all measures of hand function. Among these, the strongest correlation is between cognition and bimanual performance (r=0.354). See Figure 1 for boxplots and scatter plots visualizing the correlations.

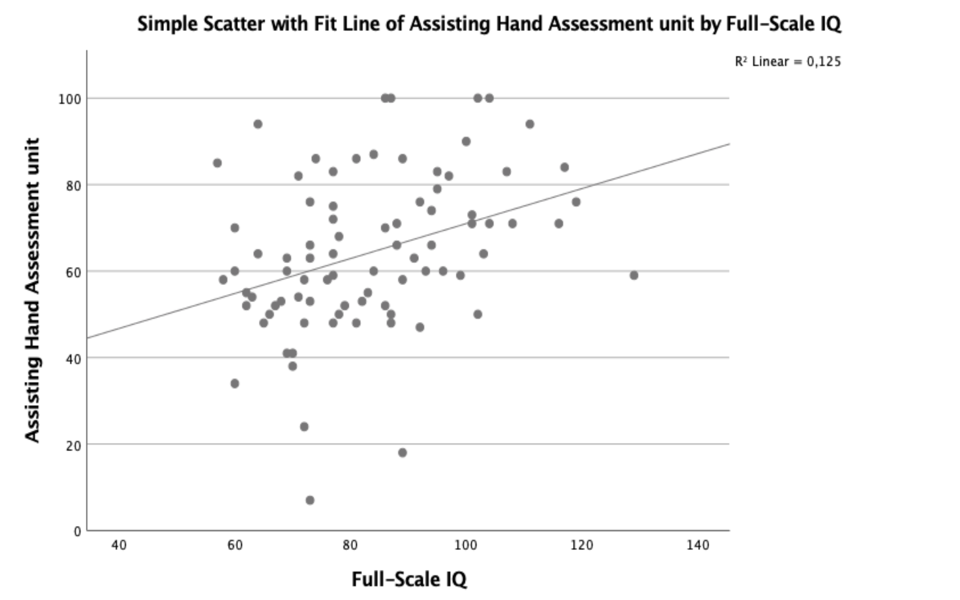
Figure 1: Correlation between the bimanual performance measured with Assisting Hand Assessment (AHA) and Manual Ability Classification System (MACS), active use of the affected hand classified with the House Functional Classification (House) and cognition measured as full-scale IQ (FSIQ).

Correlation between AHA unit and MACS



Correlation between AHA unit and House



Correlation between AHA and FSIQ	

AHA unit= Assisting Hand Assessment unit; MACS= Manual Ability Classification System; House= House Functional Classification, FSIQ= Full-Scale IQ (WPPSI & WISC)

Relationship between IQ and hand function

A linear regression-analysis was selected to investigate the associations between bimanual performance as the dependent variable, and manual ability, active use of the affected hand and cognition as independent variables. In addition, sex and age were entered into the model, but did not contribute to the model and were therefore removed. Table 4 shows the results from multiple regression analysis from all the variables.

Table 4. Model illustrating strengths and explanatory power between bimanual performance and manual ability, cognition and active use of the affected hand.

	Standardized coefficients				
Model	β	t	Significance	95% CI for β	r^2 (% variance)
Constant		3.0	0.003		
House	0.5	6.4	0.000		
MACS	-0.2	-3.1	0.002		0.64
FSIQ	0.7	0.9	0.323		

Dependent variable: AHA unit
AHA Unit=Assisting Hand Assessment unit; House=House Functional Classification; FSIQ=Full-Scale IQ (WPPSI & WISC).

The model shows that both House for the affected hand and manual ability classified with MACS significantly contributed to the model, but cognition (FSIQ) did not. Therefore, FSIQ was removed from the model and a new linear regression analysis was performed to examine the strengths and explanatory power between bimanual performance, active use of the affected hand (House) and manual ability. The results indicate that active use of the affected hand and MACS, significantly contributed to the model and accounted for 65% of the variance in the AHA unit (see Table 5.) This means that cognition did not contribute to the variance in AHA unit, but also that 35% of the variance in bimanual performance is explained by other variables that have not been examined.

Table 5. Results of multiple regression analysis for bimanual performance in children with unilateral cerebral palsy

			Standardized coefficients		
Model	β	t	Significance	95% CI for β	r^2 (% variance)
Constant		4.5	0.000		
House affected hand	0.6	6.7	0.000		0.65
MACS	-0.3	-3.4	0.001		

Dependent variable: AHA unit
AHA unit= Assisting Hand Assessment unit; House= House Functional Classification; MACS= Manual Ability Classification System

Correlation between the five indexes in the Wechsler tests and bimanual performance

Data from the five indexes and AHA were available for 41 children. The Pearson *r* correlation analysis were selected to investigate the correlation between bimanual performance and the five indexes: Verbal Comprehension Index (VCI), Visual Spatial Index (VSI), Fluid Reasoning Index (FRI), Working Memory Index (WMI), and Processing Speed Index (PSI). and hand function.

Table 6. Pearson r correlations between the five indexes and AHA

	AHA unit	**VCI**	**VSI**	**FRI**	**WMI**	**PSI**
AHA unit	-	0.197	0.337**	0.305*	0.323*	0.448**
VCI	0.197	-	0.474**	0.685**	0.624**	0.503**
VSI	0.337**	0.474**	-	0.774**	0.696**	0.639**
FRI	0.305*	0.685**	0.774**	-	0.686**	0.663**
WMI	0.323*	0.624**	0.696**	0.686**	-	0.590**
PSI	0.448**	0.503**	0.639**	0663**	0.590**	-

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

AHA unit= Assisting Hand Assessment unit; WMI= Working Memory Index; FRI= Fluid Reasoning Index; VSI= Visual Spatial Index; VCI= Verbal Comprehension Index; PSI= Processing Speed Index.

Table 6 show that there is a significant correlation between all the variables, except between bimanual performance and Verbal Comprehension Index. The strongest correlation is between bimanual performance and Processing Speed Index (r=0.448), while the correlations between working memory (WMI), fluid reasoning (FRI) and visual-spatial cognition (VCI) is significant, but weaker.

Relationship between the five indexes and bimanual performance

A linear regression-analysis was performed to investigate the strengths and explanatory power between bimanual performance as the dependent variable and the five indexes as independent variables to see if these variables significantly contributed to the model, in addition to House classification of the affected hand and MACS. None of the five indexes contributed significantly to the model, meaning the results indicate that the five indexes did not contribute to the variance in bimanual performance.

Discussion

In this population-based study we investigated the association between cognition and bimanual performance in children with spastic unilateral CP. Our results indicate that there is a moderate correlation between full-scale IQ and bimanual performance, However, full-scale IQ does not seem to be a significant factor when it comes to explaining the variance in bimanual performance. To our knowledge, no research has examined the relationship between IQ measured with the Wechsler tests and bimanual performance measured with AHA before. Additionally, research on the relationship between cognition and bimanual performance in children with CP, especially spastic unilateral CP is scarce (8). Furthermore, general measures of intelligence offer a broad-based assessment of intellectual ability, but are not sensitive to specific cognitive impairments seen in children with CP (24). It is therefore possible that the Wechsler tests do not detect specific cognitive impairments that can affect bimanual performance in children with spastic unilateral CP.

Nevertheless, our results indicate that there is a strong positive correlation between active use of the affected hand and bimanual performance and a strong negative correlation between manual ability and bimanual performance. In addition, both active use of the affected hand and manual ability seem to significantly contribute to 65% of the variance in bimanual performance.

Our findings regarding the relationship between active use of the affected hand and bimanual performance supports similar research on unimanual capacity and bimanual performance. In Sakzewski et al. (53) study, the relationship between unimanual capacity (Melbourne Assessment of Unilateral Upper Limb Function (MUUL)) and bimanual performance (AHA) in children with congenital hemiplegia were examined. The results showed a strong relationship between unimanual capacity bimanual performance. Additionally, unimanual capacity and stereognosis accounted for 75% of variance in bimanual performance. However, our findings does not support some of the results in Klingels, et al. (54) study where the aim was to examine the time course of upper limb function in children with unilateral CP over a five-year follow-up. The results indicated that despite improvements in unimanual capacity, the bimanual performance deteriorated. This was seen in children from the age of nine and older, where they used their affected hand less and less efficiently in bimanual activities.

The results in this current study show a strong relationship between manual ability and bimanual performance, which is similar to Klevberg et al. (55) study, where they described the development of bimanual performance in young children with unilateral or bilateral CP. In this study their results indicate that children´s manual ability classified with MACS level may predict future development of bimanual performance, meaning manual ability is strongly associated with bimanual performance.

The data from the children used in this current study are from the population of children with spastic unilateral CP in Norway. As expected, there were more males than females with unilateral CP (56). The included children classified across MACS levels I-III, which closely resembles what earlier research has reported (5, 17). Nevertheless, most of the included children classified in MACS level II, whereas most of the children in the total population classified in MACS level I. This is not uncommon, as there are studies that have had both a majority of children classifying at MACS level I, but also a majority of children classifying at MACS level II (5, 10). However, there were six children in the total population that classified at MACS level IV, which is uncommon for children with spastic unilateral CP (57). Most of the participants in this current study had either a white matter injury or a grey matter injury, which is similar with reports from recent research (33). Regarding active use in the affected hand classified with House, 32.5 % of the included group had only reduced dexterity or no limitations in the affected hand, nevertheless 48.2% had poor to good active grasp. These findings are not similar to the findings in Arner, et al. (57) study, where most of the children with spastic unilateral CP classified in levels 7-8 (only reduced dexterity or no limitations in the affected hand) , and a few children classified at level 4-6 (poor to good active grasp). Still, there was a close resemblance on all comparable demographic variables between the included and excluded participants in this current study, meaning this allows for some generalization of the results.

The secondary aim was to explore the strength of the associations between bimanual performance and the five cognitive index scores: Verbal Comprehension Index (VCI), Visual Spatial Index (VSI), Fluid Reasoning Index (FRI), Working Memory Index (WMI), and Processing Speed Index (PSI).

The results in this current study showed a significant, but weak correlation between bimanual performance and VSI, FRI, WMI and PSI, but the strongest correlation was between processing speed (PSI) and bimanual performance (AHA). There was no correlation between bimanual performance and Verbal Comprehension Index. However, our results indicate that none of the indexes significantly contributed to the variance in bimanual performance. To our knowledge, this current study is the first to examine the relationship between the Indexes in the Wechsler tests and bimanual performance. Therefore, one can conclude that the cognitive functions measured in these indexes does not have a significantly effect on bimanual performance, but there may be other cognitive components such as executive function, that has an effect on bimanual performance. Earlier research describes children with unilateral spastic CP of having slightly lower overall level of cognitive functioning and attention (58), additionally to problems related to visual-spatial cognition, acquisition of visual imagery and executive functioning (36). Executive function involves inhibition of inappropriate or automatic responses, initiation and planning of behaviour, multi-tasking, cognitive flexibility, judgement and decision making, and monitoring performance (59). We were unable to examine the relationship between executive function and bimanual hand function in children with spastic unilateral CP, which possible can affect performance in everyday activities (8). Therefore, future studies should consider examining this relationship and its impact on performance and participation in everyday activities for children with spastic unilateral CP.

Study limitations

The limitations in this study include the small group size of children assessed in cognitive function with the Wechsler tests. Furthermore, there were not enough data on children assessed with BRIEF (The Behaviour Rating Inventory of Executive Function). Therefore, we could no examine the relationship between executive function and bimanual performance.

Acknowledgements

I am deeply honoured to have had the opportunity to write my Master´s thesis with this project at the Norwegian University of Science and Technology (NTNU). I am especially grateful to my supervisor, Ann-Kristin Elvrum, for her invaluable mentoring, guidance, advices, and knowledge in this project. I would also like to give my gratitude to neuropsychologist, Kristine Stadskleiv, for her contribution in this thesis, by transforming the scaled scores to standardized scores in the WISC-V and WPPSI-IV, and for all her invaluable inputs. I would like to thank CPRN and CPOP for providing me the data used in this thesis, and to all the children and their parents for their valuable contributions to increasing knowledge about this population.

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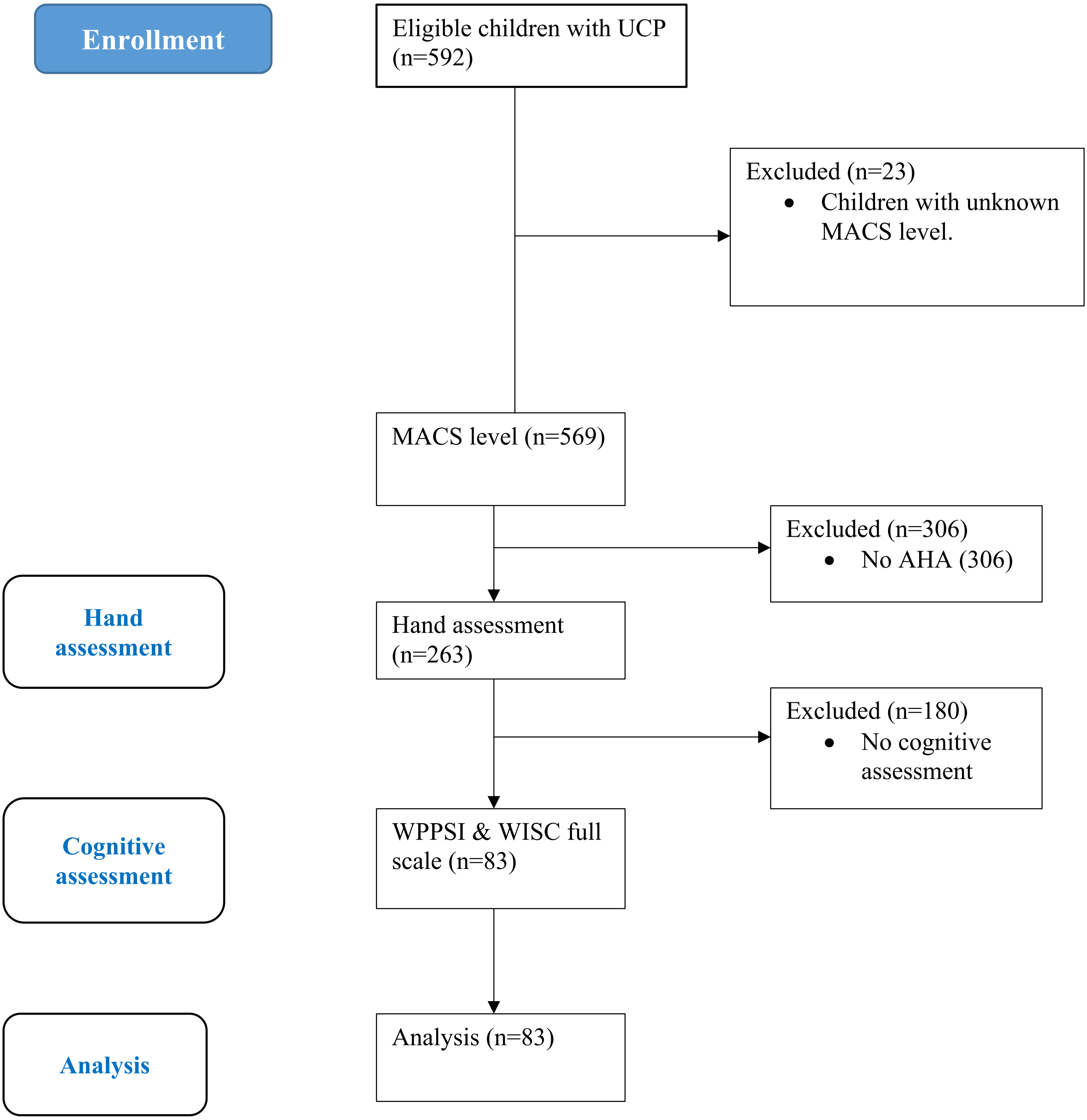
Appendix 1- Study flow chart of the inclusion-process

Study Flow Chart



Appendix 2. Guidelines from Scandinavian Journal of Occupational Therapy

Full length research articles:

- Should be written with the following elements in the following order: title page; abstract; keywords main test introduction, materials and methods, results, discussion; Methodological considerations/limitations; acknowledgments; declaration of interest statement; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figures; figures captions (as a list).
- An average article should be around 5000 words but can be up to a maximum of 8500 words.
- Should contain a structured abstract of 200 words. Background, Aims/Objectives, Material and Methods, Results, Conclusions and Significance.
- Between 3 and 10 keywords.
- The **introduction** should explain the background of the study grounded in updated literature. The rationale of study should be stated and the significance for occupational therapy explained. The aim of the study should be clearly described.
- The **material and methods** section should give sufficient detail to enable other investigators to repeat the work. Describe new methods in detail. The design and investigated population should be appropriate for the research problem stated and aim of the study. Consider reliability/validity or trustworthiness of the instruments and procedures. Use appropriate statistical and qualitative analyses and procedures. Ethical considerations should be accounted for.
- The **results** section should be concise and focus on findings relevant to the aim of the study. When relevant, use pertinent quotations as illustrations to qualitative findings. Figures and tables should be adequately annotated and enhancing the presentation of material. Avoid presenting data in more than one form.
- The **discussion** section should give critical assessment of the results of the study in view of previously reported research. Conclusions in relation to the aim should be stated likewise the significance of findings for occupational therapy. Avenues for future research should be suggested. Methodological considerations/limitations should be acknowledged.
- **Acknowledgments -** State funding and sources of support in the form of e.g. grants or equipment on a separate Acknowledgements page.
- Please use British (-ize) spelling style consistently throughout your manuscript.

Appendix 3. REK approval

Alle skriftlige henvendelser om saken må sendes via REK-portalen
Du finner informasjon om REK på våre hjemmesider rekportalen.no

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK midt	Magnus Alm	73559949	07.05.2020	94904
			Deres referanse:	

Ann-Kristin Gunnes Elvrum

94904 Kognisjon og håndfunksjon hos barn med unilateral cerebral parese - en populasjonsbasert studie

Forskningsansvarlig: Norges teknisk-naturvitenskapelige universitet

Søker: Ann-Kristin Gunnes Elvrum

REKs vurdering

Vi viser til søknad om prosjektendring datert 27.04.2020 for ovennevnte forskningsprosjekt. Søknaden ble behandlet av sekretariat for REK midt på fullmakt, med hjemmel i helseforskningsloven § 11 og forskrift om behandling av etikk og redelighet i forskning § 10.

Det søkes om følgende endringer:

-Endring i utvalg: En kan ikke identifisere hvem som har fylt 16 år i CP-registeret, og det er dermed vanskelig å etterkomme REKs vilkår om passivt samtykke fra disse. Man skal derfor bare inkludere personer som ikke har fylt 16 år i studien.

-Ny prosjektmedarbeider: Kristine Stadskleiv, Oslo universitetssykehus HF.

Vurdering

REK midt har vurdert søknad om prosjektendring, og har ingen forskningsetiske innvendinger mot endringen av prosjektet. Hensynet til deltakernes velferd og integritet er fremdeles godt ivaretatt.

Vedtak

Godkjent

Med vennlig hilsen

Hilde Eikemo
Sekretariatsleder, REK midt

Magnus Alm
rådgiver, REK midt

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK midt. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK midt, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag (NEM) for endelig vurdering.

NTNU

Norwegian University of
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