Assessment of bimanual performance in 3-D movement analysis Validation of a new clinical protocol in children with unilateral cerebral palsy

Thibault Pasquet, Armel Crétual, Hélène Rauscent, Isabelle Bonan, Florence Gaillard, Marine Cacioppo, Brice Bouvier, Guillaume Bouzillé, Christopher J Newman

Assessment of bimanual performance in 3-D movement analysis: validation of a new clinical protocol in children with unilateral cerebral palsy

Florence Gaillard[1,2]*, Marine Cacioppo[1]*, Brice Bouvier[2], Guillaume Bouzille[3,4], Christopher J. Newman[5], Thibault Pasquet[1], Armel Cretual[2], Hélène Rauscent[1], Isabelle Bonan[1]

1. Department of Physical Medicine and Rehabilitation, Rennes University Hospital, 35033 Rennes, France

2. M2S laboratory (Mouvement Sport Santé), Rennes 2 University – ENS Rennes - UEB, Campus de Ker Lann, 35170 Bruz, France

3. INSERM U1099, Rennes, F-35000, France

4. CIC Inserm 1414. Centre de Données Cliniques, Rennes University Hospital, 35033 Rennes, France

5. Paediatric Neurology and Neurorehabilitation Unit, Lausanne University Hospital, Nestlé Hospital, CHUV, 1011 Lausanne, Switzerland

* These authors contributed equally to this work.

Corresponding author

Florence Gaillard,

Rennes University Hospital

Physical Medicine and Rehabilitation

2 Rue Henri Le Guilloux

35033 Rennes,

FRANCE; florence-gaillard@hotmail.fr

Abstract

Background. The "Be an Airplane Pilot" (BE-API) protocol is a novel 3-D movement analysis (3DMA) protocol assessing the bimanual performance of children during a game.

Objective. This study aimed to investigate the reliability and validity of this protocol in children with unilateral cerebral palsy (uCP).

Methods. Angular waveforms (WAVE), maximum angles (MAX) and range of motion (ROM) of the trunk, shoulder, elbow and wrist joints were collected in children with uCP and in typically developing children (TDC) during 4 tasks of the BE-API protocol designed to explore specific degrees of freedom (DoF). The inter-trial reliability was assessed with the coefficient of multiple correlation (CMC) for WAVE and the intraclass correlation coefficient (ICC) and standard error of measurement (SEM) for MAX and ROM. Clinical performance-based measures, including the Assisting Hand Assessment (AHA) and ABILHAND-Kids scores, were used to explore correlations between clinical measures and kinematic parameters in children with uCP.

Results. For the 20 children with uCP (13 boys; mean age 12.0 [SD 3.2] years) and 20 TDC (11 boys; mean age 11.9 [SD 3.4] years), most kinematic parameters showed high reliability (WAVE: CMC ≥ 0.82; MAX and ROM: ICC ≥ 0.85, SEM $\leq 4.7°$). Elbow extension, forearm supination, and wrist adduction were reduced and wrist flexion was increased for children with uCP versus TDC ($p<0.01$). In children with uCP, MAX and ROM values were moderately correlated with clinical assessments (AHA score: r = 0.48-0.65; ABILHAND-Kids score: r = 0.48-0.49).

Conclusions. The BE-API protocol is a 3DMA bimanual performance-based assessment that is highly reliable in children with uCP. Children with uCP and TDC significantly differed in some clinically relevant kinematic parameters. The BE-API is a promising playful tool, helpful for better understanding upper-limb motor movement abnormalities in bimanual conditions and for tailoring treatments to individual deficits.

Keywords. Unilateral cerebral palsy; 3-D movement analysis; upper limb; bimanual task; bimanual performance

Introduction

Disorders of the upper limb (UL), such as sensorimotor deficits, spasticity [1], synkinetic movements [2], coordination disorders and difficulties in motor planning [3], are common in children with unilateral cerebral palsy (uCP) due to a brain lesion. These deficiencies impair the grasping and manipulation of objects. In daily activities, children with uCP have more difficulties in bimanual situations (e.g., buttoning a shirt, tying laces, opening a bottle) than other children because the activities require interaction and coordination between both hands [4].

Beyond unimanual capacity (i.e., what the child can do best with the impaired hand), clinicians need to assess bimanual performance (i.e., how the child spontaneously uses the impaired UL during bimanual tasks) in order to plan treatments and ultimately improve the child's autonomy. Among the existing clinical rating tools, the Assisting Hand Assessment (AHA) [5] and the ABILHAND-Kids [6] scores are considered the best performance-based measures available to evaluate bimanual activity in children with uCP [7]. However, these clinical measures are exposed to operator's subjectivity, with a risk of lacking reliability. Indeed, the results of their psychometric properties were recently questioned [8]. Moreover, they do not provide an accurate description of the movement of the impaired UL.

An objective and quantitative description of impaired UL during bimanual activities can be obtained with 3-D movement analysis (3DMA). 3DMA is commonly used as a gold-standard clinical tool to assess the kinematics of lower limbs during gait [9]. The extension of 3DMA to the UL in clinical practice is challenging, notably because of the large degrees of freedom (DoF), the lack of cyclic movements and the variety of activities performed (reach/grasp/manipulate, unimanually/bimanually, symmetrically/asymmetrically). Most UL 3DMA studies have focused on movement of the impaired UL during unimanual activities (reach, grasp or gross motor tasks) [10–14], assessing the child's unimanual capacity and not bimanual performance.

Few studies have evaluated bimanual performance with a set of bimanual tasks in children with uCP. Klotz et al. [15] reported increased movement time and restricted range of motion (ROM) of pronation but did not explore wrist movement. Rudisch et al. [16] measured spatial and temporal parameters during a unique bimanual box task but did not explore any joint angle data. In addition, none of these works assessed reliability, which is an essential step before deployment into clinical practice.

This paper introduces a new 3DMA protocol, “Be an Airplane Pilot” (BE-API), used to assess bimanual performance during a series of 4 child-friendly tasks. This protocol explores all the DoF of the UL known as limited in children with uCP [12–14], under various bimanual conditions and within functional ROM [17].

The aim of this study was to assess the inter-trial reliability and validity of the BE-API protocol in children with uCP. The validation involved comparison with data from typically developing children (TDC) (discriminative ability) and correlations with clinical measures including the AHA and ABILHAND-Kids scores (concurrent validity).

Material and methods

Participants

We recruited children with uCP from the Physical Medicine and Rehabilitation Department of Rennes University Hospital who were age 6 to 18 years and could actively handle an object (Manual Ability Classification System [MACS] level I to III [18]). Exclusion criteria included UL pain, severe cognitive or visual disturbances, previous UL surgery and/or use of botulinum toxin during the past 6 months. Children with uCP were compared to TDC, who performed the BE-API protocol, under exactly the same conditions as the children with uCP.

Ethical approval was granted by the local ethics committee. Written informed consent was obtained from all parents and children for this study.

Clinical measurements

Two clinical performance-based measures of bimanual activities recommended in the literature [7] were used to evaluate bimanual performance in children with uCP: the AHA [5] and the ABILHAND-Kids [6] questionnaire. The AHA is a playful session assessing the spontaneous use of the impaired UL during bimanual tasks; the video-recorded session is rated by an operator trained and certified for AHA. The scores range from 0 to 100 AHA-units, 100 AHA-units corresponding to optimal spontaneous use of the assisting hand. The ABILHAND-Kids is a questionnaire completed by parents for assessing manual daily performance. The score is expressed in %-logits; a high score corresponds to good manual daily performance.

BE-API protocol

3-D marker tracking involved using a 12-camera Optitrack sampling at 100 Hz (Motion Analysis, Corvallis, OR, USA). A 26-marker set was applied on the trunk, arms, forearms and hands according to the recommendations of the International Society of Biomechanics (ISB) [19] with markers adapted to the anthropometry of the children (9 mm). Four extra markers were applied on the different objects of the set-up to ease the detection of movement cycles.

Participants were seated on a height-adjustable chair with the hips and knees at a 90° angle in front of a height adjustable table, with elbows flexed at a 90° angle and hands resting on the table surface. All settings and position of objects (i.e., joystick, turbo, buzzers 1 and 2) were adjusted according to the child's anthropometry (Fig. 1).

The 3DMA protocol is a game called "Be an Airplane Pilot" (BE-API protocol) consisting of 4 bimanual tasks described and illustrated in Supplementary Material I. These tasks were conceived to largely mobilize DoF that are often limited in the impaired UL of children with uCP [12–14]: elbow extension and wrist adduction (Task 1, "mountain passing"), shoulder elevation and rotation (Task 2, "slaloming"), shoulder plane of elevation and wrist extension (Task 3, "dropping parachutists") and forearm supination (Task 4, "refueling"). These targeted DoF, called "primary DoF" in this study, were mobilized in ROMs consistent for daily life activities [17]. The other DoF, solicited to a lesser extent and possibly participating in movement compensations, were also analysed and were called "secondary DoF". The primary and secondary DoF explored during the 4 tasks are presented in Figure 2.

In a trial, 4 consecutive cycles of movement were performed for tasks 1, 2 and 3. One cycle of movement was performed for Task 4 ("refueling") after each of tasks 1 to 3, to maintain a playful link between these 3 tasks and to keep the game immersion. Thus, the chronological order of 1 trial was: Task 1 (4 cycles) – Task 4 (1 cycle) – Task 2 (4 cycles) – Task 4 (1 cycle)

– Task 3 (4 cycles) – Task 4 (1 cycle). In a session, 3 consecutive trials were performed by the child at a self-selected speed.

Data selection and kinematic parameter extraction

Selection of movement cycles for analysis were chosen before the experimentation, based on the literature [11]. Regarding tasks 1, 2 and 3, in which movements were successively performed 4 times, only the second and third cycles were kept to avoid any bias of start/stop strategies. Task 4 corresponds to a unique cycle performed after tasks 1, 2 and 3; these 3 cycles were retained. Considering a session, 6 selected movements for tasks 1, 2 and 3 (2 cycles x 3 trials) and 9 selected movements for Task 4 (3 cycles x 3 trials) were analysed (Supplementary Material II).

The kinematics of the trunk (flexion-extension, lateral flexions and rotations), shoulder (elevation, plane of elevation, rotations), elbow (flexion-extension and prono-supination) and wrist (flexion-extension and abduction-adduction) were calculated by using the Euler sequences recommended by the ISB [19]. The shoulder joint was defined as the "thoracohumeral joint" and its joint center was estimated by using a functional method [20,21]. The kinematic data were processed by using Matlab (MathWorks, Natick, MA, USA).

The angular waveform (WAVE), maximum angle value (MAX) and ROM were calculated for all primary and secondary DoF.

Statistical analysis

All statistical tests were performed with $p<0.05$ considered statistically significant (R v3.3.3).

The first series of analyses examined the inter-trial reliability of the kinematic parameters. The inter-trial reliability of WAVE involved estimating the coefficient of multiple correlation (CMC) between the 6 (for tasks 1, 2 and 3) and 9 (for Task 4) selected movements, from which median values were calculated for every child, with 95% confidence intervals (CIs) [22]. Four mean CMC thresholds were considered: excellent (≥0.90), good (0.80–0.89), moderate (0.60–0.79), and poor (<0.60) [23]. The inter-trial reliability of MAX and ROM was assessed with the intraclass correlation coefficient (ICC(2k)) and the standard error of measurement (SEM)[23,24]. Mean values were reported with 95% CIs. Four ICC thresholds were considered: very high (≥0.80), moderately high (0.60–0.79), moderate (0.40–0.59), and low (<0.40).

The second series of analyses tested whether the uCP and TDC groups differed in kinematic parameters. The uCP and TDC groups were compared on each kinematic parameter of the hemiplegic/non-dominant UL by using Student *t* test or Mann-Whitney U test according to the normality of the distribution. The p-values were adjusted for multiple comparisons with the false discovery rate method [25]. Effect sizes were computed by using Cohen's *d* [26], with *d* defined as the difference between the means of the 2 groups divided by the pooled standard deviation. Three thresholds of effect size were considered: large (>0.80), moderate (0.20-0.79) and low (<0.20) effect size.

The third series of analyses examined the association between the discrete angle values (ROM and MAX) and the clinical measures. Bivariate correlations with Spearman's rank correlation coefficients were calculated [27]. A correlation coefficient <0.90 was considered very high, >0.70 high, 0.50 to 0.69 moderate, 0.30 to 0.49 low, <0.30 little or no correlation.

Results

We included 20 children with uCP (13 boys; mean age 12.0 [SD 3.2] years; 7 right /13 left hemiplegia) with MACS level I (n=5), II (n=12), and III (n=3); mean AHA score 66.1 (SD 14.1) AHA-unit and mean ABILHAND-Kids score 71.8 (SD 12.7) %-logits. Children with uCP were compared to 20 TDC (11 boys; mean age 11.9 [SD 3.4] years, range 6–18 years. Children with uCP and TDC were comparable in age (*p*=.928).

Inter-trial reliability for children with uCP

Angular waveforms (Table 1)

Regarding the primary DoF, the inter-trial reliability was good for the shoulder rotation (CMC = 0.84) and wrist flexion-extension (CMC = 0.82) and excellent for the other primary DoF (CMC >0.90). Regarding the secondary DoF, all CMC values were good to excellent for tasks 1, 2 and 3, with moderate reliability for Task 4 (CMC 0.68–0.77).

ROM and MAX angle values (Table 1)

Inter-trial reliability was excellent for all primary and secondary DoF, for both ROM (ICC 0.86–0.98) and MAX (ICC 0.85–0.99). Similarly, inter-trial SEM values for ROM and MAX were < 5° for all primary and secondary DoF.

Comparison of kinematic parameters between children with uCP and TDC (Table 2)

For ROM parameters, significantly decreased values were found for primary DoF for children with uCP versus TDC, with a large effect size for wrist abduction-adduction, forearm pronosupination and shoulder rotation (Cohen's *d* >1.17). The ROM for wrist flexion-extension was greater for children with uCP than TDC, with a large effect size (Cohen's *d* =0.98). For secondary DoF, certain ROMs significantly differed between children with uCP and TDC: shoulder plane elevation, forearm pronosupination and wrist flexion-extension.

For MAX parameters, significantly decreased values were found for primary DoF for children with uCP versus TDC, with a large effect size for elbow extension, wrist adduction and forearm supination (Cohen's *d*>1.03). MAX values were significantly higher for children with uCP for wrist flexion, with a large effect size (*Cohen's d*=1.03). For secondary DoF, MAX values were lower for children with uCP for shoulder plane elevation (anterior plane), with a large effect size (Cohen's *d* >0.89).

Correlation between kinematic parameters and clinical measures (Table 3)

We found low to moderate significant correlations between AHA score and the following primary DoF: MAX of wrist adduction and wrist flexion and ROM and MAX of shoulder plane elevation. Some secondary DoF were moderately and significantly correlated with AHA score: positive correlation with ROM of wrist flexion-extension, MAX of wrist extension and ROM of shoulder rotations, and negative correlation with ROM of trunk rotations.

For the primary DoF, ROM and MAX for shoulder plane elevation showed moderate and low correlation with the ABILHAND-Kids score. For secondary DoF, MAX of trunk rotations showed low to moderate correlation with the ABILHAND-Kids score.

Discussion

This study introduces a novel 3DMA protocol, called BE-API, that allows for objectively assessing the performance of the impaired UL in children with uCP during playful bimanual activities. Unlike gait, the assessment of bimanual performance is challenging because there is not just one UL function. The 4 clinically relevant tasks of the BE-API protocol were designed to 1) assess the DoF of the non-dominant UL, known as limited in children with uCP [12–14], 2) in functional ranges of motion required in daily life activities [17] and 3) in various conditions of movement (symmetrical or asymmetrical tasks, defined or free trajectories, manipulation of different objects that were grasped or pushed). The originality of this protocol is the integration of these bimanual tasks into a playful scenario. Masking the clinical setting with a game environment induced total adherence by children with uCP and improved their spontaneity of movements [28]. All children with uCP showed very good participation, especially those 6 to 12 years old who really appreciated the game immersion. All children performed all sessions of the BE-API protocol, without tiredness or lack of concentration.

All DoF for the main 3 joints of the UL (wrist, elbow, shoulder) were explored, contrary to previous studies in which the wrist was not included [12,15,29].

The BE-API protocol demonstrated a high level of inter-trial reliability for both angular waveforms and kinematic parameters (MAX and ROM) during the 4 tasks, as well as or better than the previous unimanual protocol exploring reliability [30]. The rigorous standardization of the playful scenario led to spontaneous reliability, each child reproducing his/her own motor strategies for each trial. We found low values of measurement error (SEM <5°) for the MAX and ROM of all DoF. These results agree with a previous unimanual study [30], which suggests that the BE-API protocol is sensitive to measure the DoF known as limited in children with uCP and can be used as a reliable tool for clinical implementation.

The BE-API protocol highlighted kinematic differences in children with uCP as compared with TDC (discriminative ability). In distal joints, children with uCP had lower elbow extension, forearm supination, wrist adduction and higher wrist flexion than TDC. These findings are consistent with similar studies using unimanual tasks [12–14,31] and bimanual tasks [16,29].

In proximal joints, children with uCP had restricted shoulder rotations and plane of elevation as compared with TDC, as was shown previously [11,29]. We found no significant difference in shoulder elevation, but restricted elevation of shoulder was reported during unimanual reach tasks [11,14]. This finding has 2 explanations. First, the tasks described in the literature required wider shoulder motion, as far as an anatomical maximum, which allowed for detecting greater differences between children with uCP and TDC. In our study, we evaluated how children spontaneously mobilized their joint during a functional task, less demanding in terms of ROM performed. Second, a subgroup study focused on MACS subgroups might highlight more deviated values of ROM and MAX in the MACS III group versus MACS II and I groups, as shown by Mailleux et al. for shoulder mobility [32]. However, the small size of our sample (MACS III, n=3) did not allow us to test this hypothesis.

Trunk mobility was explored as secondary DoF to highlight possible compensatory movement. No significant difference between groups was found. This finding can be explained by the position of the table placed in contact with the child's abdomen in order to limit the lower trunk moving forward.

The BE-API protocol demonstrated its discriminative ability, highlighting significant kinematic differences in children with uCP versus TDC during bimanual activities. Like gait analysis, these UL movement abnormalities must be interpreted with clinical measurements (e.g., muscle strength, spasticity, passive ROM) to deduce the underlying neuromotor deficiencies. These deficiencies, such as muscle weakness of the wrist or elbow extensors and/or hypertonia of forearm pronators, elbow and/or wrist flexors [1,33,34], are commonly targeted by therapies, such as botulinum toxin injection or neuro-orthopedic surgery [35]. Thus, the BE-API protocol is a promising objective tool to better understand the mechanisms of UL impairments during bimanual activities, to tailor target therapeutics and to assess the effectiveness of these treatments.

The concurrent validity of the BE-API protocol was explored by the correlation between kinematic parameters (ROM and MAX) and clinical based-performance measures (AHA and ABILHAND-Kids scores). To our knowledge, only Mailleux et al. [32], who used a unimanual protocol, investigated the relation between kinematic parameters and AHA score. We found significant moderate correlations between the AHA score and several angle measures (wrist extension and flexion, wrist adduction, shoulder plane of elevation and trunk rotation), similar to Mailleux et al. [32], and significant correlations between kinematic parameters and the ABILHAND-Kids score, especially for proximal joints (trunk and shoulder), whereas Klotz et al. [15] found no consistent correlation.

These correlation findings are promising, but better correlations could be expected. One explanation could be the limitations of the clinical tools, whose psychometric properties were questioned in a recent study [8], suggesting that their sensitivity and reliability have not been strongly proven. In future studies, correlations with clinical tools that have strong psychometric properties, such as the revised version of the AHA (5.0) [36], would be more relevant. Moreover, as demonstrated in a previous study [32], kinematic indices, such as the Arm Profile Score [37], were better correlated with the AHA than the ROM and MAX. Taking into account other kinematic parameters, such as comparison between the uCP waveform and the average for TDC [37,38] and/or speed, movement efficiency and smoothness [39], could provide better correlation with clinical measures and would allow a more complete evaluation of the impaired UL during bimanual tasks. As illustrated in Supplementary Material III*,* the waveform of the child with uCP differed from the average waveform of TDC. Statistical Parametric Mapping, recently used in movement analysis [38], is a valid method to compare entire waveforms between children with uCP and TDC. Used in further studies, this method would allow for investigating specific UL movement patterns and better understanding the influence of distal motor impairments, such as spasticity or muscle weakness.

Some limitations must be discussed. First, we noticed in the per-protocol that Task 2, "slaloming", was impossible to perform for the youngest child with MACS level III because of the continuous grip needed with the impaired hand throughout the task and his distractibility due to his young age (7 years old). The ergonomy of the joystick could be improved to facilitate the grip of the object. Second, the small sample size and the distribution of MACS levels did not allow for further statistical analysis in subgroups, such as reliability or kinematic abnormalities according to MACS level or age. A further study is necessary including a larger group of children sampled across the different MACS levels.

Conclusions

The BE-API protocol is an innovative 3DMA performance-based assessment of the impaired UL in children with uCP that involves a game scenario with bimanual tasks. This protocol was successfully performed by children with uCP with very high inter-trial reliability.

Children with uCP and TDC significantly differed in some clinically relevant kinematic parameters, at the level of wrist, elbow and shoulder. Such a 3DMA-bimanual protocol is promising to better understand the UL movement abnormalities in children with uCP and to tailor treatments to individual deficits. Future work will involve investigating the between-day reliability and exploring the movement patterns of the UL based on the waveforms.

Acknowledgements. We thank the children and families, the team of the Paediatric Physical Medicine and Rehabilitation department of Rennes University Hospital and the M2S laboratory.

Conflict of interest. None declared.

Legends

Figure 1. A child in the "Be an Airplane Pilot" (BE-API) protocol set-up. A 26-marker set was applied on the trunk, arms, forearms and hands according to the recommendations of the International Society of Biomechanics.

Figure 2. Primary (big black dots) and secondary (small white dots) degrees of freedom (DoF) of the non-dominant upper limb and the trunk explored with each task. Flex, flexion; Ext, extension; Int, internal; Ext, external; Abd, abduction; Add, adduction; DoF, degrees of freedom.

References

[1] Rosenbaum P, Paneth N, Leviton A, Goldstein M, Bax M, Damiano D, et al. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol Suppl. févr 2007;109:8-14.

[2] Kuhtz-Buschbeck JP, Sundholm LK, Eliasson A-C, Forssberg H. Quantitative assessment of mirror movements in children and adolescents with hemiplegic cerebral palsy. Developmental Medicine & Child Neurology. 2000;42(11):728-36.

[3] Steenbergen B, Gordon AM. Activity limitation in hemiplegic cerebral palsy: evidence for disorders in motor planning. Dev Med Child Neurol. sept 2006;48(9):780-3.

[4] Eliasson AC, Burtner PA. Improving hand function in children with cerebral palsy : theory, evidence and intervention. London: MacKeith Press; 2008. p160-75 p.

[5] Krumlinde-Sundholm L, Holmefur M, Kottorp A, Eliasson A-C. The Assisting Hand Assessment: current evidence of validity, reliability, and responsiveness to change. Dev Med Child Neurol. avr 2007;49(4):259-64.

[6] Arnould C, Penta M, Renders A, Thonnard J-L. ABILHAND-Kids: a measure of manual ability in children with cerebral palsy. Neurology. 28 sept 2004;63(6):1045-52.

[7] Klingels K, Jaspers E, Van de Winckel A, De Cock P, Molenaers G, Feys H. A systematic review of arm activity measures for children with hemiplegic cerebral palsy. Clin Rehabil. oct 2010;24(10):887-900.

[8] Gerber CN, Labruyère R, van Hedel HJA. Reliability and Responsiveness of Upper Limb Motor Assessments for Children With Central Neuromotor Disorders: A Systematic Review. Neurorehabilitation and Neural Repair. janv 2016;30(1):19-39.

[9] Gage JR. Gait analysis. An essential tool in the treatment of cerebral palsy. Clin Orthop Relat Res. mars 1993;(288):126-34.

[10] Butler EE, Ladd AL, Louie SA, LaMont LE, Wong W, Rose J. Three-dimensional kinematics of the upper limb during a Reach and Grasp Cycle for children. Gait & Posture. mai 2010;32(1):72-7.

[11] Jaspers E, Desloovere K, Bruyninckx H, Klingels K, Molenaers G, Aertbeliën E, et al. Three-dimensional upper limb movement characteristics in children with hemiplegic cerebral palsy and typically developing children. Research in Developmental Disabilities. nov 2011;32(6):2283-94.

[12] Mackey AH, Walt SE, Stott NS. Deficits in Upper-Limb Task Performance in Children With Hemiplegic Cerebral Palsy as Defined by 3-Dimensional Kinematics. Archives of Physical Medicine and Rehabilitation. févr 2006;87(2):207-15.

[13] Fitoussi F, Diop A, Maurel N, Laassel EM, Penneçot GF. Kinematic analysis of the upper limb: a useful tool in children with cerebral palsy. J Pediatr Orthop B. juill 2006;15(4):247-56.

[14] Coluccini M, Maini ES, Martelloni C, Sgandurra G, Cioni G. Kinematic characterization of functional reach to grasp in normal and in motor disabled children. Gait & Posture. avr 2007;25(4):493-501.

[15] Klotz MCM, van Drongelen S, Rettig O, Wenger P, Gantz S, Dreher T, et al. Motion analysis of the upper extremity in children with unilateral cerebral palsy—An assessment of six daily tasks. Research in Developmental Disabilities. nov 2014;35(11):2950-7.

[16] Rudisch J, Butler J, Izadi H, Zielinski IM, Aarts P, Birtles D, et al. Kinematic parameters of hand movement during a disparate bimanual movement task in children with unilateral Cerebral Palsy. Human Movement Science. avr 2016;46:239-50.

[17] Gates DH, Walters LS, Cowley J, Wilken JM, Resnik L. Range of Motion Requirements for Upper-Limb Activities of Daily Living. Am J Occup Ther. 2016;70(1):7001350010p1-10.

[18] Eliasson A-C, Krumlinde-Sundholm L, Rösblad B, Beckung E, Arner M, Ohrvall A-M, et al. The Manual Ability Classification System (MACS) for children with cerebral palsy: scale development and evidence of validity and reliability. Dev Med Child Neurol. juill 2006;48(7):549-54.

[19] Wu G, van der Helm FCT, (DirkJan) Veeger HEJ, Makhsous M, Van Roy P, Anglin C, et al. ISB recommendation on definitions of joint coordinate systems of various joints for the reporting of human joint motion—Part II: shoulder, elbow, wrist and hand. Journal of Biomechanics. mai 2005;38(5):981-92.

[20] Gamage SSHU, Lasenby J. New least squares solutions for estimating the average centre of rotation and the axis of rotation. Journal of Biomechanics. janv 2002;35(1):87-93.

[21] Lempereur M, Leboeuf F, Brochard S, Rousset J, Burdin V, Rémy-Néris O. In vivo estimation of the glenohumeral joint centre by functional methods: Accuracy and repeatability assessment. Journal of Biomechanics. janv 2010;43(2):370-4.

[22] Kadaba MP, Ramakrishnan HK, Wootten ME. Measurement of lower extremity kinematics during level walking. J Orthop Res. mai 1990;8(3):383-92.

[23] Jaspers E, Feys H, Bruyninckx H, Harlaar J, Molenaers G, Desloovere K. Upper limb kinematics: Development and reliability of a clinical protocol for children. Gait & Posture. févr 2011;33(2):279-85.

[24] Weir JP. Quantifying test-retest reliability using the intraclass correlation coefficient and the SEM. J Strength Cond Res. févr 2005;19(1):231-40.

[25] Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society: Series B (Methodological). janv 1995;57(1):289-300.

[26] Cohen J. A power primer. Psychol Bull. juill 1992;112(1):155-9.

[27] Hinkle DE, Wiersma W, Jurs SG. Applied Statistics for the Behavioral Sciences. 5 edition. Boston: Houghton Mifflin; 2002. 756 p.

[28] Volman MJM, Wijnroks A, Vermeer A. Effect of task context on reaching performance in children with spastic hemiparesis. Clin Rehabil. sept 2002;16(6):684-92.

[29] Klotz MCM, Kost L, Braatz F, Ewerbeck V, Heitzmann D, Gantz S, et al. Motion capture of the upper extremity during activities of daily living in patients with spastic hemiplegic cerebral palsy. Gait & Posture. mai 2013;38(1):148-52.

[30] Jaspers E, Feys H, Bruyninckx H, Cutti A, Harlaar J, Molenaers G, et al. The reliability of upper limb kinematics in children with hemiplegic cerebral palsy. Gait & Posture. avr 2011;33(4):568-75.

[31] Reid S, Elliott C, Alderson J, Lloyd D, Elliott B. Repeatability of upper limb kinematics for children with and without cerebral palsy. Gait & Posture. mai 2010;32(1):10-7.

[32] Mailleux L, Jaspers E, Ortibus E, Simon-Martinez C, Desloovere K, Molenaers G, et al. Clinical assessment and three-dimensional movement analysis: An integrated approach for upper limb evaluation in children with unilateral cerebral palsy. Kellermayer MS, éditeur. PLOS ONE. 3 juill 2017;12(7):e0180196.

[33] Gordon AM, Duff SV. Relation between clinical measures and fine manipulative control in children with hemiplegic cerebral palsy. Developmental Medicine & Child Neurology. 1999;41(9):586-91.

[34] Gorter JW, Rosenbaum PL, Hanna SE, Palisano RJ, Bartlett DJ, Russell DJ, et al. Limb distribution, motor impairment, and functional classification of cerebral palsy. Developmental Medicine & Child Neurology. 2004;46(7):461-7.

[35] Boyd RN, Morris ME, Graham HK. Management of upper limb dysfunction in children with cerebral palsy: a systematic review. Eur J Neurol. nov 2001;8 Suppl 5:150-66.

[36] Holmefur MM, Krumlinde-Sundholm L. Psychometric properties of a revised version of the Assisting Hand Assessment (Kids-AHA 5.0). Developmental Medicine & Child Neurology. 2016;58(6):618-24.

[37] Jaspers E, Feys H, Bruyninckx H, Klingels K, Molenaers G, Desloovere K. The Arm Profile Score: A new summary index to assess upper limb movement pathology. Gait & Posture. juin 2011;34(2):227-33.

[38] Simon-Martinez C, Jaspers E, Mailleux L, Desloovere K, Vanrenterghem J, Ortibus E, et al. Negative Influence of Motor Impairments on Upper Limb Movement Patterns in Children with Unilateral Cerebral Palsy. A Statistical Parametric Mapping Study. Front Hum Neurosci [Internet]. 5 oct 2017 [cité 15 avr 2019];11. Disponible sur: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5633911/

[39] Butler EE, Ladd AL, LaMont LE, Rose J. Temporal–spatial parameters of the upper limb during a Reach & Grasp Cycle for children. Gait & Posture. juill 2010;32(3):301-6.

CLM-19-16143_R3

Community-acquired bacterial meningitis in adults: in-hospital prognosis, long term disability and determinants of outcome in a multicentre prospective cohort

Sarah Tubiana[1], Emmanuelle Varon[2], Charlotte Biron[3], Marie-Cecile Ploy[4], Bruno Mourvillier[5], Muhamed-Kheir Taha[6], Mathieu Revest[7], Claire Poyart[8], Guillaume Martin-Blondel[9], Marc Lecuit[10], Eric Cua[11], Blandine Pasquet[12], Marie Preau[13], Bruno Hoen[14]*, Xavier Duval[15]* and the COMBAT study group.

* These authors contributed equally

1 Sarah Tubiana, ST: Paris University, IAME, INSERM, F-75018 Paris, France; Inserm Clinical Investigation Center 1425, Paris, France. sarah.tubiana@aphp.fr

2 Emmanuelle Varon, EV: National Reference Centre for Pneumococci, Centre Hospitalier Intercommunal de Créteil, Créteil, France.

3 Charlotte Biron, CB : Infectious Diseases Department, CHU Hôtel Dieu and INSERM UIC 1413 Nantes University, Nantes, France

4 Marie-Cécile Ploy, MCP : CHU Limoges, Observatoires Régionaux du Pneumocoque, Limoges, France.

5 Bruno Mourvillier, BM: Medical and Infectious Diseases Intensive Care Unit, AP-HP, Bichat Hospital, Paris University, Paris, France.

6 Muhamed-Kheir Taha, MKT: Institut Pasteur, Invasive Bacterial Infections Unit, National Reference Centre for Meningococci and Haemophilus Influenza, Paris, France.

7 Mathieu Revest, MR: Infectious diseases and Intensive care Unit, Inserm U 1230, CHU Rennes, Rennes University, F-35033 Rennes, France

8 Claire Poyart, CP: Department of Bacteriology, University Hospitals Paris Centre-Cochin, French National Center for Streptococci, APHP, France.

9 Guillaume Martin-Blondel, GMB: CHU de Toulouse, Service des Maladies Infectieuses et Tropicales, Toulouse, F-31300 France ; INSERM, UMR1043, Toulouse, F-31300 France.

10 Marc Lecuit, ML: Institut Pasteur, Biology of Infection Unit, Inserm U1117, National Reference Center and WHO Collaborating Center for Listeria, Paris, France. Université de Paris, Hôpital Universitaire Necker-Enfants Malades, Service des Maladies Infectieuses et Tropicales, Institut Imagine, APHP, Paris-France

11 Eric Cua, EC: Infectious Diseases Department, CHU Nice, France

12 Blandine Pasquet, BP: Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Unité de Recherche Clinique Paris Nord, F-75018 Paris, France.

13 Marie Preau, MP: GRePS, Lyon 2 University, Lyon, France.

14 Bruno Hoen, BH : CHU de Nancy, hôpitaux de Brabois, service de maladies infectieuses et tropicales, 54511 Vandœuvre-lès-Nancy cedex, France.

15 Xavier Duval, XD: Paris University, IAME, INSERM, F-75018 Paris, France; Inserm Clinical Investigation Center 1425, Paris, France; Inserm, F-CRIN, Innovative clinical research network in vaccinology (I-REIVAC), Paris, France

Running title: Outcome of bacterial meningitis

Abstract (250 words)

Objectives. To identify factors associated with unfavorable in-hospital outcome (death or disability) in adults with community-acquired bacterial meningitis (CABM).

Methods. In a prospective multicenter cohort study (COMBAT; February 2013-July 2015), all consecutive cases of CABM in the 69 participating centers in France were enrolled and followed up for 12 months. Factors associated with unfavorable outcome were identified by logistic regression and long-term disability analyzed.

Results. Among the 533 enrolled patients, (*S. pneumoniae* 53.8% (280/520 isolates identified), *N. meningitidis* 21.3% (111/520), others 24.9% (129/520)), case fatality rate was 16.9% (90/533) and unfavorable outcome occurred in 45.0% (225/500). Factors independently associated with unfavorable outcome were: age > 70 years (aOR=4.64; 95%CI [1.93-11.15]), male gender (aOR=2.11; [1.25-3.57]), chronic renal failure (aOR=6.65; [1.57-28.12]), *purpura fulminans* (aOR=4.37; [1.38-13.81]), localized neurological signs (aOR=3.72; [2.29-6.05]), disseminated intravascular coagulation (aOR=3.19; [1.16-8.79]), cerebrospinal fluid (CSF) white-cell count < 1500 cells/µL (aOR=2.40; [1.42-4.03]), CSF glucose concentration (0.1-2.5g/L: aOR=1.92; [1.01-3.67]; <0.1g/L: aOR=2.24; [1.01-4.97]), elevated CSF protein concentration (aOR=1.09; [1.03-1.17]), time interval between hospitalization and lumbar puncture > 1 day (aOR=2.94; [1.32-6.54]), and *S. pneumoniae* meningitis (aOR=4.99 ; [1.98-12.56]), or meningitis other than *N. meningitidis* (aOR=4.54; [1.68-12.27]). At twelve months, 26.7% (74/277) had hearing loss, 32.8% (87/265) depressive symptoms, 31.0% (86/277) persistent headache, and 53.4% had a Physical HRQL (142/266) < 25th percentile of the distribution of the score in the general French population (p<0.0001).

Conclusions. The burden of CABM (death, disability, depression, impaired quality of life, and hearing loss) is high. Identification of cases from the first symptoms may improve prognosis.

Introduction

Community-acquired adult bacterial meningitis (CABM) is a rare disease with an annual incidence around 2/100 000 inhabitants, affecting all age groups and responsible for high morbidity and mortality [1–3]. The epidemiology of community-acquired bacterial meningitis has changed after the introduction of conjugate vaccines [3–5]. Therapeutic challenges, particularly poor penetration of antibiotics into the cerebrospinal fluid and bacterial strains with decreased susceptibility to antibiotics make management complex. Recent therapeutic improvements have mainly relied on the adjunctive use of dexamethasone, whose indications differ according to guidelines [6–9]. Guidelines also differ regarding the antibiotic treatment of meningitis caused by pneumococci with reduced susceptibility to third-generation cephalosporins; only the French recommendations are recommending very high doses of cephalosporins without the systematic addition of vancomycin [9].

Despite meningitis high morbidity and mortality, few large studies have evaluated either the determinants of in-hospital mortality-morbidity or the long-term consequences: disability, quality of life, and depressive symptoms in discharged patients [10–12]. This prospective cohort was designed to describe epidemiological, clinical, and management profiles of adult patients with CABM, with the objective of identifying factors associated with in-hospital unfavorable outcome, and assessing outcome and quality of life one year after diagnosis.

Methods

Study design and setting

The COMBAT study is a national prospective multicenter cohort study in which adults with CABM were consecutively enrolled in 69 hospitals between February 2013 and July 2015.

Participants

Eligible patients were adults (age ≥18) presenting with a CABM or a *purpura fulminans*. CABM was defined by at least one of the following 1) a CSF culture positive for bacteria; 2) the combination of CSF pleocytosis with a positive blood culture or a positive CSF PCR or antigen test for a meningitis-causing bacterium; or 3) the identification of *Neisseria meningitidis* by culture or specific PCR from a skin biopsy in case of petechiae.

Procedures

In each center, patients were pre-enrolled in the study. Patients or their legal representatives received written information about the study. Only those who gave consent were definitely enrolled. Clinical and microbiological data were prospectively collected and strains were sent to the corresponding national reference centers (see Supplementary Methods). Patients were followed up throughout hospitalization and were contacted by phone twelve months after enrollment. For patients lost to follow-up, vital status was obtained using the French Epidemiology Centre on Medical Causes of Death (CepiDc) database.

Variables

Neurological examinations were performed immediately upon enrollment and before discharge. In-hospital outcome was graded at discharge according to the modified Rankin Scale [13,14]. The primary endpoint was unfavorable in-hospital outcome, defined by a score of 2–6 (i.e., slight to severe disability, or death) on the modified Rankin scale at discharge [15].

At twelve months, depressive symptoms were assessed using the Center for Epidemiologic Studies Depression (CES-D) scale [16], hearing loss using Hearing Handicap Inventory for the Elderly-screening version (HHIE-S) (see Supplementary Methods). Health-related quality of life (HQRL) was evaluated using the SF-12 Health Survey . Two composite scores can be derived from the SF-12 Health Survey: a Physical Component Summary (PCS) and a Mental Component Summary (MCS) HRQL score. An individual was defined as having a “impaired” physical (or mental) HRQL if his PCS (or MCS) was lower than the 25th percentile of the distribution of the score in the general French population of the same age group and gender, using an existing approach to clinically interpret the results [17-18].

Statistical methods

First, a descriptive analysis was performed in the cohort population and according to the most frequent causative microorganism (*S. pneumoniae* and *N. meningitidis*). Categorical variables were summarized as counts (percentage) and frequency distributions were compared with the Chi square test or the Fisher exact test as appropriate. Continuous variables were expressed as median (IQR) and differences were tested with the independent t-test for normally distributed variables or the Mann-Whitney U test otherwise.

Second, we searched for factors associated with an unfavorable in-hospital outcome among the following variables: patient’s background characteristics, initial clinical presentation (from symptoms onset to 48 hours after inclusion), biological results at inclusion, causative microorganisms and initial treatments [3,12]. We assessed the linearity of the association between continuous variables and outcome with the Lemeshow goodness of fit and by visual inspection. If there was no linear relationship, the continuous variable was categorized for further analyses. We estimated univariable crude ORs using logistic regression on complete cases. In the multivariate analyses, we used multiple imputations using the SAS statistical software (PROC MI) to impute missing values on all variables of interest. Variables included in the imputation models were those included in the multivariable model and those related to patient clinical course. We used fully conditional specification (FCS) method with linear regression for continuous variables and with discriminant function for categorical variables. We obtained ORs estimates for the multivariate logistic regression model by averaging results across 30 imputed datasets using Rubin's rules [19]. All variables were entered into multivariate model without using any method of selecting variables. Goodness of fit was evaluated by the Hosmer–Lemeshow test and the predicted probabilities validation by c-statistic. The statistical tests were two-tailed; we estimated Wald confidence limits and we deemed p values of less than 0.05 as statistically significant.

We also aimed to identify factors associated with unfavorable in-hospital outcome separately for *S. pneumoniae* and *N. meningitidis* and to identify factors associated with in-hospital death. All statistical analyses were performed using SAS version 9.4 software (SAS Institute Inc., Cary, NC).

Ethics and regulatory issues

This study was registered with ClinicalTrials.gov (NCT02916732) and received ethics approval by the Comité de Protection des Personnes Ile de France CPP 4 (IRB 00003835) (2012-16NI), and the French Data Protection Authority (Commission nationale de l'informatique et des libertés) - (EGY/FLR/AR128794).

Results

Patient's characteristics

A total of 533 patients with bacterial meningitis were enrolled with median age of 58.4 [42.0-68.5] years male sex accounted for 55.2% (294/533; sex ratio: 1.2) (Figure 1; Table 1). Patients with pneumococcal meningitis were older (median 60.2 years, IQR [48.4–68.3]) than those with meningococcal meningitis (median age 30.0 years, IQR [21.4–56.0]) p<0. 001) (Table S1). Risk factors were noted in 353/527 (67.0%) patients and included alcoholism in 83 patients (15.9%), diabetes in 77 (14.8%), CSF leak in 66 (12.6%), history of cancer in 54 (10.3%), immunosuppressant drug use in 21 (4.0 %), or prior splenectomy in 16 patients (3.0%).

Initial clinical presentation from symptoms onset to 48 hours after inclusion

An episode of influenza-like illness prior to meningitis diagnosis was less frequently reported in patients with pneumococcal (91/270; 33.7%) than meningococcal meningitis (56/108; 51.9%) (p=0.001). Antibiotics had been administered during the 48 hours preceding hospital admission to 36.2% (188/520) patients (Table 1). Seizures before hospitalization, fever and altered mental status were all more likely to occur in pneumococcal than in meningococcal meningitis (Table 1).

Distant foci of infection (otitis or sinusitis n=147, pneumonia n=55 or endocarditis n=27) and localized neurological signs were more frequent in patients with pneumococcal than meningococcal meningitis (54.3% vs 6.3%; p<0.0001 and 39.6% vs 22.5%; p=0.0014 respectively)(Table S1).

Cerebrospinal fluid findings and brain imaging

The median time interval [Q1; Q3] between the meningitis symptom onset and the lumbar puncture was 1 day [1-3]. All CSF laboratory parameters are displayed in Table 1. CSF Gram staining was positive in 366/521 (70.2%) episodes, 228/276 (82.6%) of pneumococcal meningitis, 73/107 (68.2%) of meningococcal meningitis, 12/32 (37.5%) of *Listeria* meningitis and 21/36 (58.3%) of other streptococcal meningitis.

Figure 2:

	DoF	**Task 1** Mountain passing 	**Task 2** Slaloming 	**Task 3** Dropping parachutists 	**Task 4** Refueling 
TRUNK	Flex-Ext	○			
	Rotations Int-Ext			○	
SHOULDER	Elevation	○	●		
	Plane Elevation		○	●	○
	Rotations Int-Ext		●	○	○
ELBOW	Flex-Ext	●			
	Prono-Supination		○	○	●
WRIST	Flex-Ext	○	○	●	○
	Abd-Add	●			

Table 1. Inter-trial reliability of the waveforms (WAVE), range of motion (ROM) and maximum angles (MAX) parameters for each task of the “Be an Airplane Pilot” protocol.

		DoF	Task 1				Task 2				Task 3				Task 4			
			Angular value (°) [SD]	CMC [95% CI]	ICC [95% CI]	SEM (°) [95% CI]	Angular value (°) [SD]	CMC [95% CI]	ICC [95% CI]	SEM (°) [95% CI]	Angular value (°) [SD]	CMC [95% CI]	ICC [95% CI]	SEM (°) [95% CI]	Angular value (°) [SD]	CMC [95% CI]	ICC [95% CI]	SEM (°) [95% CI]
TRUNK	ROM	Flex-Ext	24.7 [8.7]	0.95 [0.92–0.97]	0.91 [0.78–0.96]	2.8 [1.7–4.2]												
		Rot Int-Ext									19.8 [5.9]	0.95 [0.95–0.96]	0.94 [0.87–0.97]	1.5 [1.1–1.9]				
	MAX	Flexion	24.4 [7.1]		0.95 [0.89–0.97]	1.6 [1.2–2.1]												
		Ext Rot									14.2 [8.8]		0.97 [0.93–0.98]	1.6 [1.2–2.0]				
SHOULDER	ROM	Elev	32.7 [8.0]	0.98 [0.97–0.99]	0.95 [0.86–0.98]	1.8 [1.5–2.3]	32.0 [6.1]	0.96 [0.95–0.97]	0.88 [0.79–0.93]	2.3 [1.8–2.8]								
		Plane Elev					37.5 [12.3]	0.93 [0.90–0.95]	0.88 [0.81–0.93]	4.4 [2.7–6.0]	77.9 [15.4]	0.97 [0.95–0.98]	0.96 [0.91–0.98]	2.9 [2.0–3.8]	19.9 [10.3]	0.73 [0.63–0.81]	0.95 [0.88–0.97]	2.4 [1.7– 3.0]
		Rot Int-Ext					26.6 [13.5]	0.84 [0.79–0.88]	0.91 [0.76–0.96]	4.3 [2.6–6.6]	39.4 [10.0]	0.93 [0.90–0.96]	0.86 [0.72–0.93]	4.0 [3.0–5.2]	33.2 [15.3]	0.77 [0.66–0.86]	0.97 [0.92– 0.99]	2.7 [1.9–3.4]
	MAX	Elev	85 [9.7]		0.95 [0.89–0.98]	2.2 [1.5–3.0]	68.7 [9.7]		0.92 [0.82–0.96]	2.7 [2.1–3.4]								
		Plane Elev post									18.3 [11.3]		0.92 [0.72–0.97]	3.3 [2.1–4.7]				
		Plane Elev ant					83 [15.4]		0.92 [0.84–0.96]	4.4 [2.8–5.9]					59 [11.2]			0.96 [0.91–0.98]
		Int Rot									-9.5 [16.2]		0.95 [0.85–0.98]	3.8 [2.9–4.9]				
		Ext Rot					62.8 [19.0]		0.96 [0.89–0.98]	4.1 [2.9–5.5]					61.3 [15.8]			0.97 [0.94–0.98]

ELBOW	ROM	Flex-Ext	36.5 [10.5]	0.93 [0.87–0.97]	0.87 [0.61–0.95]	4.2 [2.8–6.3]												
		Prono-Sup					66.7 [19.1]	0.96 [0.93–0.97]	0.94 [0.87–0.97]	4.7 [3.3–6.3]	33.2 [10.9]	0.88 [0.84–0.91]	0.89 [0.71–0.95]	3.8 [3.0–4.9]	77.8 [23.1]	0.92 [0.87–0.95]	0.98 [0.97–0.99]	3.1 [1.8–4.5]
	MAX	Extension	-45.2 [10.2]		0.92 [0.69–0.99]	3.1 [1.3–5.6]												
		Pronation									38.8 [12.0]		0.97 [0.93–0.98]	2.2 [1.8–2.7]				
		Supination					37.1 [16.5]		0.95 [0.90–0.97]	3.7 [2.6–4.9]					40.7 [27.3]		0.98 [0.96–1.00]	3.3 [1.26–5.4]
WRIST	ROM	Flex-Ext	30.9 [12.3]	0.93 [0.85–0.97]	0.90 [0.66–0.96]	3.8 [2.7–5.8]	45.6 [16.6]	0.95 [0.93–0.97]	0.97 [0.85–0.99]	3.0 [2.2–4.0]	31.8 [11.6]	0.82 [0.78–0.87]	0.91 [0.80–0.96]	3.6 [2.7–4.8]	18.3 [9.6]	0.68 [0.59–0.76]	0.94 [0.82–0.98]	2.4 [1.8–3.1]
		Abd-Add	22.2 [6.8]	0.97 [0.96–0.98]	0.95 [0.88–0.98]	1.5 [1.2–1.9]												
	MAX	Flexion	19 [6.3]		0.91 [0.82–0.95]	2.4 [1.9–3.1]					21.4 [17.8]		0.97 [0.93–0.98]	3.3 [2.5–4.0]				
		Extension					32.6 [23.5]		0.99 [0.95–1.00]	2.4 [1.8–3.0]					10.3 [12.2]		0.98 [0.95–0.99]	1.8 [1.3–2.3]
		Add	28.2 [7.5]		0.85 [0.71–0.92]	1.4 [0.9–1.8]												

Data are mean [SD] angular values and mean coefficient of multiple correlation (CMC), intraclass correlation coefficient (ICC) and standard error of measurement (SEM) with 95% confidence intervals (CIs) for primary DoF (dark grey) and secondary DoF (light grey).

Abd, abduction; Add, adduction; Ant: anterior; DoF, degrees of freedom; Elev, elevation; Ext, extension; Ext rot, external rotation; Flex, flexion; Int rot, internal rotation; Post: posterior; Prono-sup, prono-supination.

Table 2. Comparison of ROM and MAX values for primary DoF (dark grey) and secondary DoF (light grey) between children with unilateral cerebral palsy (uCP) and typically developing children (TDC).

		DoF	Task 1				Task 2				Task 3				Task 4			
			uCP	**TDC**	***p*-value**	**Cohen's *d***	**uCP**	**TDC**	***p*-value**	**Cohen's *d***	**uCP**	**TDC**	***p*-value**	**Cohen's *d***	**uCP**	**TDC**	***p*-value**	**Cohen's *d***
TRUNK	ROM	Flex-Ext	24.7 [8.7]	27.5 [8.1]	0.387†	0.33												
		Rotations									19.8 [5.9]	16.4 [4.0]	0.068†	0.69				
	MAX	Flexion	24.4 [7.1]	26.7 [8.1]	0.478†	0.30												
		Ext Rot									14.2 [8.8]	14.2 [4.8]	0.957‡	0.00				
SHOULDER	ROM	Elev	32.7 [8.0]	37.9 [6.1]	0.052†	0.74	32.0 [6.1]	35.7 [9.0]	0.295‡	0.47								
		Plane Elev					37.5 [12.3]	56.2 [13.9]	**0.001†**	**1.43**	77.9 [15.4]	84.5 [11.6]	0.223†	0.48	19.9 [10.3]	27.7 [10.1]	0.052†	0.77
		Rot Int-Ext					26.6 [13.5]	47.8 [21.8]	**0.004†**	**1.17**	39.4 [10.0]	37.7 [12.5]	0.674†	0.15	33.2 [15.3]	37.2 [13.2]	0.459†	0.28
	MAX	Elevation	85.0 [9.7]	88.9 [10.4]	0.445†	0.38	68.7 [9.7]	71.8 [10.0]	0.478†	0.31								
		Plane Elev post									18.3 [11.3]	19.7 [9.9]	0.919‡	0.13				
		Plane Elev ant					83 [15.4]	103.8 [11.4]	**<0.001†**	**1.54**					59.0 [11.2]	68.1 [9.2]	**0.026†**	**0.89**
		Int Rot									-9.5 [16.2]	-5.1 [13.3]	0.478†	0.30				
		Ext Rot					62.8 [19.0]	77.6 [19.7]	0.058†	0.77					61.3 [15.8]	63.3 [14.9]	0.767†	0.13

ELBOW	ROM	Flex-Ext	36.5 [10.5]	42.1 [12.8]	0.223†	0.48												
		Prono-Sup					66.7 [19.1]	59.5 [16.7]	0.295†	0.40	33.2 [10.9]	43.9 [11.3]	**0.012‡**	**0.96**	77.8 [23.1]	102.0 [10.6]	**0.002‡**	**1.34**
	MAX	Extension	-45.2 [10.2]	-32.5 [6.7]	**<0.001†**	**1.47**												
		Pronation									38.8 [12.0]	42.1 [11.9]	0.504†	0.27				
		Supination					37.1 [16.5]	41.2 [10.1]	0.478†	0.30					40.7 [27.3]	63.8 [6.0]	**0.009‡**	**1.16**
WRIST	ROM	Flex-Ext	30.9 [12.3]	32.9 [10.5]	0.634†	0.18	45.6 [16.6]	55.3 [8.6]	**0.010‡**	0.73	31.8 [11.6]	22.0 [8.1]	**0.012‡**	**0.98**	18.3 [9.6]	17.5 [5.6]	0.736‡	0.11
		Abd-Add	22.2 [6.8]	29.9 [5.5]	**0.002†**	**1.23**												
	MAX	Flexion	19.0 [6.3]	15.2 [7.7]	0.138‡	0.53					21.4 [17.8]	7.8 [6.1]	**0.009†**	**1.03**				
		Extension					32.6 [23.5]	39.5 [7.0]	0.767‡	0.40					10.3 [12.2]	14.9 [5.0]	0.264†	0.50
		Add	28.2 [7.5]	34.1 [3.2]	**0.009†**	**1.03**												

Data are mean [SD].

Significant differences between groups were determined by *t* test [†] or Mann-Whitney U test [‡].

Abd, abduction; Add, adduction; Ant: anterior; Elev, elevation; Ext, extension; Ext rot, external rotation; Flex, flexion; Int rot, internal rotation; Post: posterior; Prono-sup, prono-supination.

Table 3. Correlation (Spearman rank correlation coefficients) between kinematic parameters (ROM, MAX) and clinical measures (Assisting Hand Assessment [AHA], ABILHAND-Kids) for children with uCP. Only correlations > 0.30 are displayed.

ROM			MAX		
	AHA	ABILHAND-Kids		AHA	ABILHAND-Kids
Task 1					
Tr flexion-extension	-	-0.33	Tr Flexion	-	-
Sh Elevation	-	-	Sh Elevation	-	-
Elb flexion-extension	-	0.32	**Elb Extension**	-	-
Wri flexion-extension	0.49*	-	Wri Flexion	-	0.30
Wri abduction-adduction	-0.31	-	**Wri Adduction**	0.48*	-
Task 2					
Sh Elevation	-	-	**Sh Elevation**	-	-
Sh Plane Elevation	-	-	Sh Plane Elevation	-	-
Sh Rotations	-	-	**Sh Ext Rotation**	-	-
Elb Prono-supination	-	0.33	Elb Supination	-	-
Wri flexion-extension	0.62**	-	Wri Extension	0.51*	-
Task 3					
Tr Rotations	-0.50*	-0.58**	Tr Ext Rotation	-	-0.36
Sh Plane Elevation	0.65**	0.49*	**Sh Plane Elevation**	0.52*	0.48*
Sh Rotations	0.51*	-	Sh int Rotation	0.36	-
Elb Prono-supination	-	-	Elb Pronation	-	0.43
Wri flexion-extension	-0.41	-0.42	**Wri Flexion**	-0.54*	-0.35
Task 4					
Sh Plane Elevation	-	-0.35	Sh Plane Elevation	-	-
Sh Rotations	-	-	Sh Ext Rotation	-	-
Elb Prono-supination	-	-	**Elb Supination**	-	-
Wri flexion-extension	-	-	Wri Extension	0.37	-

* p<.05, ** p<.01, *** p<.001. Primary DoF for each task are represented in bold.

Tr, trunk; Sh, shoulder; Elb, elbow; Wri, wrist.