Impacts of Motor Developmental Delay on the Inter-Joint Coordination Using Kinematic Synergies of Joint Angles During Infant Crawling

Li Zhang, Chun F. Deng, Yuan Liu, Lin Chen, Nong Xiao, Sheng J. Zhai, Wen S. Hou, Yu X. Chen, and Xiao Y. Wu

***Abstract*— Motor developmental delay (MDD) usually affects the inter-joint coordination for limb movement. However, the mechanism between the abnormal inter-joint coordination and MDD is still unclear, which poses a challenge for clinical diagnosis and motor rehabilitation of MDD in infant's early life. This study aimed to explore whether the joint activities of limbs during infant crawling are represented with kinematic synergies of joint angles, and evaluate the impacts of MDD on the inter-joint coordination using those synergies. 20 typically developing infants, 16 infants at risk of developmental delay, 11 infants at high risk of developmental delay and 13 infants with confirmed developmental delay were recruited for self-paced crawling on hands and knees. A motion capture system was employed to trace infants' limbs in space, and angles of shoulder, elbow, hip and knee over time were computed. Kinematic synergies were derived from joint angles using principal component analysis. Sample entropy and Spearman's rank correlation coefficients were calculated among those synergies to evaluate the crawling complexity and the symmetry of bilateral limbs, respectively. We found that the first two synergies with different contributions to the crawling movements sufficiently represented the joint angular profiles of limbs. MDD further delayed the development of motor function for lower limbs and mainly increased the crawling complexity of joint flexion/extension to some extent, but did not obviously change the symmetry of bilateral limbs. These results suggest that the time-varying kinematic synergy of joint angles is a potential index for objectively evaluating the abnormal inter-joint coordination affected by MDD.**

***Index Terms*— Infant crawling, joint angles, kinematic synergies, motor developmental delay, principal component analysis.**

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I. Introduction

MOTOR developmental delay (MDD), caused by brain injury or brain immaturity, is a special developmental disorder with a prevalence of more than 2-4 per 1000 in the general population, and this prevalence is much higher in high-risk infants [1]. Meanwhile, MDD in infants may further induce global developmental delay, cerebral palsy (CP) and some neuromuscular diseases [2]. Clinical practices show that early identification of MDD for infants is beneficial for timely intervening in their early developmental stages and effectively improving the development of motor function [3], [4]. However, the widely used scale assessment methods are relatively subjective and with low accuracy [4], [5]. Notably, abnormal motor posture is an important physiological characteristic of MDD [1], [2]. And joint angles can objectively quantify the coordination of motor posture [6], [7]. In fact, angular changes of joints regulated by the central nervous system (CNS) have been widely used to evaluate the joint coordination patterns and motor function, and kinematic synergy among multiple joints of limbs is regarded as a control strategy for motor coordination and motor function [8], [9]. Although the effects of MDD on the motor coordination have been observed among multiple joints for limb movement [8], [10], it is still unclear how MDD affects the regulation of joint angles during infant crawling due to the abnormal joint coordination patterns.

As the first CNS-controlled locomotion for most infants, hands-and-knees crawling can be characterized as the motor system controlling the dimensionality of joints and muscles in a coordinated manner [11], [12]. By importing surface electromyography (sEMG) signals recorded from muscles, the neuromuscular function for limb movement can be well assessed [13]. Xiong *et al.* observed that the development of motor function for infants was relevant to the muscular contractions and inter-limb coordination constrained by the neuromuscular control strategy during crawling [10], [11]. Gao *et al.* employed sEMG oscillation components to analyze the abnormal motor function for CP infants, and found that different frequency components of sEMG from multiple muscles were activated in different phases for typically developing (TD) and CP infants during crawling [14]. Although sEMG-based muscular activities were related to the kinetics of human body, they did not directly produce motor behaviors and were challenging to meet the requirement of robustness for complicated limb movement [15]. Studies of quantitative analysis of the crawling movements for infants were scarce [16]. Interestingly, our previous work indicated that the joint coordination patterns of limbs were different between TD and MDD infants during crawling [17], but it only quantified the temporal inter-joint coordination based on tangential velocities of joints, which provided little information about the spatial inter-joint coordination during crawling.

Joint angles with multiple degree of freedoms (DoFs) can be used to quantify the inter-joint coordination in time and space for limb movement [15], [18], [19]. Previous studies have found that compared to TD children, CP children showed increased joint angles of lower limbs during walking in order to maintain balance and ensure a smooth progression [20]. Currently, for gait analysis, the inter-joint coordination assessed by joint angles is mainly in the lower limbs of children with independent walking abilities and adults [8], [18], [21]. For those infants without independent walking abilities, hands-and-knees crawling is more suitable to measure the mechanisms of inter-joint coordination [11]. However, inter-joint coordination during infant crawling is rarely noted in this field [16]. Righetti *et al.* observed that the angular changes of shoulder/ hip in the sagittal plane or elbow/knee during a crawling cycle were similar among TD infants, and the actions of these joints, such as retracting during swing and protracting during stance, were related to a common principle underlying neural control [22]. It has also been suggested that the abnormal changes of joint angles during human movement can reveal the impaired motor control of the CNS and provide insight for the development of rehabilitation strategies [8], [20]. Therefore, the quantitative assessment of joint angles during infant crawling is meaningful for early detection and motor rehabilitation of MDD.

Kinematic synergy analysis is an effective way to evaluate the inter-joint coordination for limb movement [9]. Existing evidences suggest that the CNS exploits a reduced set of pre-shaped neural pathways, called synergies, to achieve different motor commands [23]. In other words, the CNS controls a few synergies that each synergy encodes multiple DoFs to simplify the control of high DoF limbs [24]. Non-negative matrix factorization (NMF) [25], singular value decomposition (SVD) [26], principal component analysis (PCA) [27] and many other algorithms have been introduced in the literatures to derive synergies for limb movement. Among them, PCA is the most frequently applied method for kinematic synergy analysis [7], [15]. PCA-derived kinematic synergies have been demonstrated to represent and generalize the hand movement kinematics favorably, compared to other linear and non-linear dimensionality reduction methods [24]. Moreover, PCA-derived kinematic synergies can effectively describe the observed physiological characteristics utilizing a small number of principal components (PCs), and provide simplified strategies for the development of motor rehabilitation and the design and control of biomimetic prosthesis [7], [15], [18]. That is, PCA-derived kinematic synergies can be effective and appropriate to analyze the physiological and pathological mechanisms of the abnormal inter-joint coordination for limb movement, and sufficiently describe the synergistic recruitment of motor modules organizing by co-varying joint angles of limbs. PCA decomposes the multi-DoF joint angles for limb movement into two components, including the time-invariant synergy weights involving the data's variance accounted for by the synergies and the time-varying synergistic patterns involving the angular amplitudes of joint abduction/adduction, flexion/extension and internal/external rotation [7], [27]. MacLellan *et al.* successfully employed the PCA algorithm to derive the time-varying kinematic synergies of joint angles for healthy young adults during crawling [19]. A few works also reported that PCA-derived kinematic synergies with different orders played different roles in human movement [7], [15], [21]. However, to our knowledge, no published studies reported the inter-joint coordination during infant crawling based on kinematic synergies of joint angles, not to mention analyzing the features of those synergies over time.

Inspired by kinematic synergy, the synergistic recruitment mechanism should be manifested with coordinated regulation of multiple joints and of different DoFs in individual joint. Thereby, we assumed that the joint activities of limbs during infant crawling could be represented with kinematic synergies of joint angles, and these multi-order synergies would exhibit different contributions to the crawling movements. Then, to quantify the features of those synergies over time, kinematic features were introduced. Since low motion complexity [28] and symmetrical limb movement [12] were typical kinematic features for healthy individuals, we expected that these features would be altered in MDD infants. At the same time, according to the asynchronous development of motor function between upper and lower limbs for infants [11], we assumed that the impaired motor control of the CNS for MDD infants would further aggravate this asynchronous process. Finally, we assumed that the effects of MDD on the inter-joint coordination could be reflected in the above metrics. To this end, we recorded the three-dimensional (3D) trajectories from multiple joints of limbs during infant crawling and derived kinematic synergies from joint angles using PCA. We also calculated the sample entropy and Spearman's rank correlation coefficients of those synergies to evaluate the crawling complexity and the symmetry of bilateral limbs, respectively.

II. Methods

A. Participants

A total of 60 infants, as listed in Table I, were recruited for this study. 40 MDD infants were recruited from the Department of Rehabilitation Center, Children's Hospital of

TABLE I
PARTICIPANT DEMOGRAPHICS

Group	Sex	Biological age (months)	Delayed age* (months)	Scale score of five dimensions assessed by GMFM-88 (%)					Number of valid crawling cycles
				Lying / rolling	Crawling / kneeling	Sitting	Standing	Walking / running / jumping	
TD (N = 20)	15 M, 5 F	11 (3)	0 (2)	92 (4.5)	54 (3.5)	85.5 (7)	27 (13.5)	12 (5.25)	5.5 (2.25)
ARDD (N = 16)	13 M, 3 F	11 (2)	1 (1)	92 (3.5)	51 (7.75)	87 (7.5)	27 (26.25)	6 (10)	5 (2.25)
AHRDD (N = 11)	7 M, 4 F	16 (3)	5 (1)	92 (1)	54 (6)	87 (4.5)	27 (21.5)	13 (17.5)	6 (4)
CDD (N = 13)	6 M, 7 F	20 (9)	10 (4)	92 (3)	54 (10)	87 (5)	24 (27)	13 (14)	8 (4)

*denotes the value determined by the Gesell Developmental Schedules. Data are expressed as median (IQR). M = male, F = female, IQR = interquartile range. IQR = 75th percentile - 25th percentile.

Chongqing Medical University. Inclusion criteria for MDD infants included: 1) biological age of <3 years old; 2) abnormal posture in hands-and-knees crawling; 3) premature delivery, low birth weight, hypoxic-ischemic brain injury at birth, or other risk factors that might affect the motor function. And 20 TD infants were recruited from local child health clinics as the control group, who were all full-term infants with normal birth weight and no other neurological diseases affecting the motor function.

All experiments were performed with informed, written consent of infants' parents or guardians in accordance with the approval of the Ethics Committee of Children's Hospital of Chongqing Medical University (approval number: 065/2011).

B. Clinical Assessment

All infants were assessed by the therapists from the Department of Rehabilitation Center, Children's Hospital of Chongqing Medical University via the Gross Motor Function Measure (GMFM-88) and Gesell Developmental Schedules. GMFM-88 measures the gross motor function, including lying/rolling, crawling/kneeling, sitting, standing and walking/running/jumping. Every function is scaled in a percentage score ranging from 0 to 100 [3]. Gesell Developmental Schedules are a set of developmental metrics, which outline the ages & stages of the development in young children [4]. To identify the motor developmental levels of infants, the delayed ages (in months) of gross motor were calculated by subtracting the developmental ages of gross motor determined by the Gesell Developmental Schedules from the biological ages (see Table I).

According to the recommendations of pediatricians from the Department of Rehabilitation Center, Children's Hospital of Chongqing Medical University, all 40 MDD infants were further divided into 3 subgroups based on the delayed ages of gross motor. Thereinto, 16 infants with a delayed age of ≤3 months were classified as infants at risk of developmental delay (ARDD), 13 infants with a delayed age of >6 months were classified as infants with confirmed developmental delay (CDD), and the remaining 11 infants were classified as infants at high risk of developmental delay (AHRDD) (see Table I). Although the biological ages of CDD group were significantly larger than those of TD, ARDD and AHRDD groups (All $p < 0.01$), the developmental ages of gross motor were similar among those 4 groups (χ^2 (3) = 3.864, p = 0.277), indicating that the movement abilities of the 4 groups were clinically comparable.

C. Experimental Protocol

A motion capture system (Raptor-E, Motion Analysis Corporation, USA) with 6 high-speed digital cameras was used to record kinematic data of every infant at 100 frames/s. Reflective markers were attached to the shoulder (lateral to the acromion), elbow (lateral epicondyle), wrist (ulnar styloid process), hip (posterior superior iliac spine), knee (lateral condyle of femur), ankle (lateral fibular malleolus), pelvis (midpoint of bilateral posterior superior iliac spine) and trunk (right scapula) (see Fig. 1a).

Before the experiments, infants were required to crawl on the floor crawling mat (360cm × 120cm) several minutes to warm up. Then, they were guided and encouraged to crawl at their own pace from one end of the mat to the opposite side (see Fig. 1a). During the experiments, infants were only allowed to wear underwear or diapers to fully expose their joints. By doing so, a set of personalized 3D trajectories of multiple joints was precisely established. A valid crawling trial required infants to crawl continuously without any perturbations at least three complete cycles.

D. Data Analysis

To evaluate the inter-joint coordination during infant crawling, multi-DoF joint angles were computed from joint trajectories, and kinematic synergies were derived from joint angles using PCA. Then, sample entropy and Spearman's rank correlation coefficients were calculated among those synergies to quantify the features of those synergies over time.

1) Pre-Processing: Kinematic data were low-pass filtered (6Hz) with a zero-lag 4th-order Butterworth filter to remove high frequency noise. Next, the cubic spline interpolation was performed for missing data in small time intervals. The locally weighted scatterplot smoothing was adopted to remove noise.

A crawling cycle was defined as an interval starting from a ground-off action of one limb and ending up with the next occurrence of the same action [16], [29]. In this study, the stance and swing phases were segmented by the squared time derivative (square of velocity) of z coordinates in the wrist/knee, and each crawling cycle began with the swing phase [14], [22]. According to our pre-experiments, a threshold

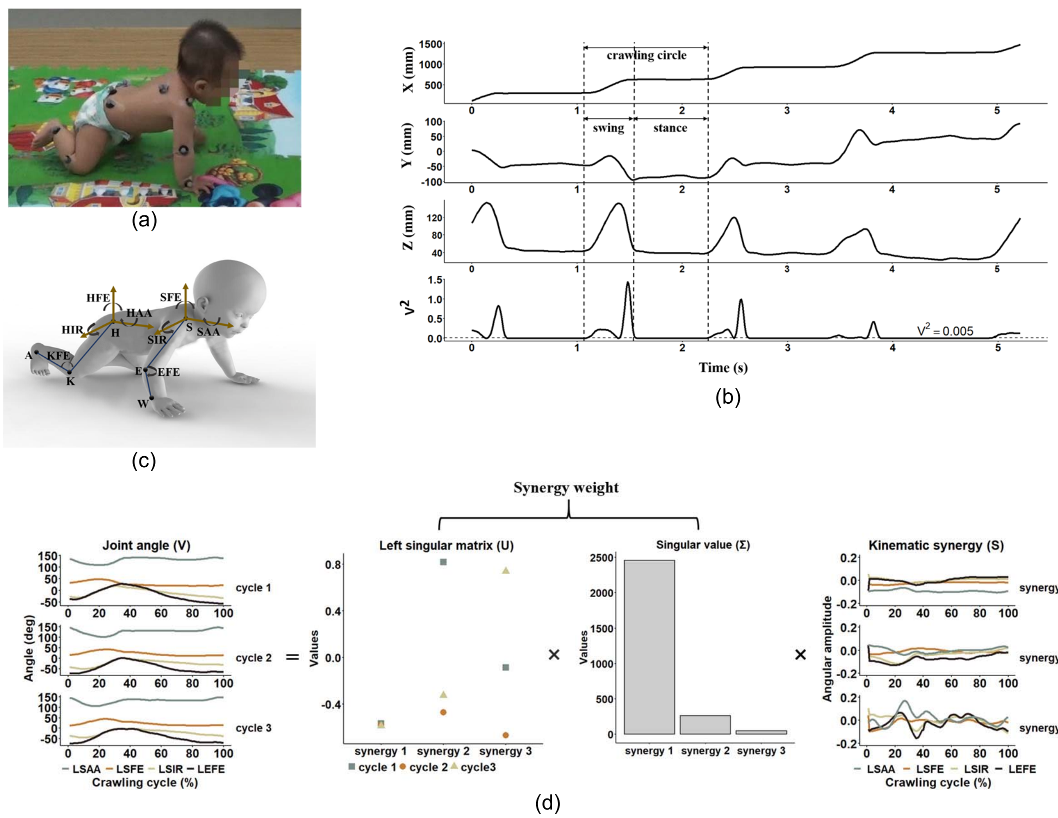


Fig. 1. (a): Snapshot of a TD infant during crawling together with the position of reflective markers. (b): Trajectories of left wrist in x-y-z coordinates and the squared time derivative (V^2, unit of velocity: m/s) of z coordinates from a TD infant during crawling. Vertical dashed lines separate the swing and stance phases during a crawling cycle. (c): Angular schematic of shoulder, elbow, hip and knee. The arrows point to the positive directions. S = shoulder, E = elbow, W = wrist, H = hip, K = knee, A = ankle, AA = abduction/adduction, FE = flexion/extension, IR = internal/external rotation. (d): Taking the left upper limb of one TD infant as an example to illustrate how joint angles are decomposed into kinematic synergistic patterns.

at 0.005 was used to determine the onset of limb movement and the end moment of each phase (see Fig. 1b). The number of valid crawling cycles for all infants varied from 3 to 15, depending on their movement abilities (see Table I).

2) Coordinate-to-Angle Transformation: The joints of limbs during infant crawling perform spatial motions [23], which can be projected on different planes. Then, these motion patterns of limbs can be evaluated by multi-DoF joint angles during infant crawling. As illustrated in Fig. 1c, the motion patterns of limbs expressed by joint angles were modeled with 4 segments: SAA, SFE, SIR and EFE of left/right upper limbs (L/RU), or HAA, HFE, HIR and KFE of left/right lower limbs (L/RL) [6], [7], [15], [26]. Because of similar calculation formulas of joint angles in the four limbs, the formulas of LU were only shown (1)–(4), at the bottom of the next page.

where $S_{x/y/z}$, $E_{x/y/z}$ and $W_{x/y/z}$ are the 3D coordinates of corresponding joints.

3) Kinematic Synergy Derivation: For further processing, the angular data during a crawling cycle were resampled from 0 to 100% (increment: 1%) for each DoF, and the swing phase was set to 40% and the stance phase was set to 60% [22]. Then, for each infant, the ith crawling cycle per limb was formatted into a 100 × 4 sub-matrix as following.

$$V_i = \begin{bmatrix} V_1^i(1) & \cdots & V_4^i(1) \\ \vdots & \ddots & \vdots \\ V_1^i(100) & \cdots & V_4^i(100) \end{bmatrix} \tag{5}$$

where the subscript (column variable) represents the joint DoFs. For each infant, 3 valid crawling cycles were analyzed due to the differences of the movement abilities. Next, 3 row matrices were used to construct a 3 × (4 × 100) matrix (V) for each limb of the infant.

$$V = \begin{bmatrix} V_1 \\ V_2 \\ V_3 \end{bmatrix} = \begin{bmatrix} V_1^1(1) & \cdots & V_4^1(1) & \cdots & V_1^1(100) & \cdots & V_4^1(100) \\ V_1^2(1) & \cdots & V_4^2(1) & \cdots & V_1^2(100) & \cdots & V_4^2(100) \\ V_1^3(1) & \cdots & V_4^3(1) & \cdots & V_1^3(100) & \cdots & V_4^3(100) \end{bmatrix} \tag{6}$$

Then, the synergistic patterns (S) were extracted from this 3 × (4 × 100) matrix (V) with PCA. Here, PCA was implemented by the SVD algorithm. Thus, three-component matrices, U, Σ and S were decomposed from V (see Fig. 1d).

$$V = U\Sigma S \tag{7}$$

where U is a 3 × 3 matrix with orthogonal columns, Σ is a 3 × 400 diagonal matrix, and S is a 400 × 400 matrix with orthogonal rows. The diagonal elements of Σ correspond to the singular values (λ_i) of V.

$$\Sigma = diag\{\lambda_1, \lambda_2, \lambda_3\} \tag{8}$$

The first m rows of S represent the first m PCs, or synergies. N is the maximal number of PCs.

$$S = \begin{bmatrix} s_1^1(1) & \cdots & s_4^1(1) & \cdots & s_1^1(100) & \cdots & s_4^1(100) \\ \vdots & \ddots & \vdots & \ddots & \vdots & \ddots & \vdots \\ s_1^m(1) & \cdots & s_4^m(1) & \cdots & s_1^m(100) & \vdots & s_4^m(100) \\ \vdots & \ddots & \vdots & \ddots & \vdots & \ddots & \vdots \\ s_1^N(1) & \cdots & s_4^N(1) & \cdots & s_1^N(100) & \vdots & s_4^N(100) \end{bmatrix} \quad (9)$$

The approximate matrix ($\widetilde{V}$) can be composed by the first m columns of U, m × m of Σ, and the first m rows of S. The matrix $U_m diag\{\lambda_1, \cdots, \lambda_m\}$ is denoted as the weight matrix for the first m synergies (S_m).

$$\widetilde{V} = U_m diag\{\lambda_1, \cdots, \lambda_m\} S_m \quad (10)$$

The cumulative percentage of explained variance (R^2) can be calculated by the first m singular values (λ_i) of Σ, which can describe how many PCs are sufficient to represent the raw data. In this study, the best number of kinematic synergies was determined by R^2 of ≥90%.

$$R^2 = \frac{\lambda_1^2 + \cdots + \lambda_m^2}{\lambda_1^2 + \cdots + \lambda_N^2} \times 100\% \quad (11)$$

4) Crawling Complexity: The crawling data of infants were the time series [13], [17], so the crawling complexity could be evaluated by the sample entropy (SE). Larger SE values indicated higher crawling complexity [28], [30], [31]. Firstly, the averaged matching number of kinematic synergies per joint DoF ({y}) was calculated as follows.

$$B_i^u(r) = \left(\text{number of } y_i \text{ such that } d\left[y_i, y_j\right] \le r\right) / (K - u) \quad (12)$$

$$B^u(r) = \frac{1}{K - u + 1} \sum_{i=1}^{K-u+1} B_i^u(r) \quad (13)$$

where $d\left[y_i, y_j\right] = \max|y_i, y_j|, i \neq j, 1 \le i, j \le K - u + 1$, K is the length of kinematic synergies per joint DoF, u represents the length of matching synergies, and r is the tolerance [28], [30]. In this study, u was set to 2, and r was equal to 0.3 multiplied by the standard deviation (SD) of ({y}) [30]. Thereby, the SE values of kinematic synergies could be denoted as follows:

$$SE = -\ln\left(\frac{B^{u+1}(r)}{B^u(r)}\right) \quad (14)$$

5) Symmetry of Bilateral Limbs: The symmetry of bilateral limbs during infant crawling is defined as the structural similarity of corresponding synergies [12]. In this study, Spearman's rank correlation coefficient was used to measure the synergy similarity [12], [31]. Larger Spearman's rank correlation coefficients indicated that the bilateral limbs were more symmetrical.

E. Statistical Analysis

Descriptive statistics include mean and SD for normal distributions, or median and IQR if not all data are normally distributed [16]. Parametric tests are conducted for comparative statistics if data sets are normally distributed and of equal variance; otherwise, nonparametric tests are used [16], [32]. In this study, one-way ANOVA (Bonferroni post hoc) and Kruskal-Wallis one-way ANOVA on ranks (Tukey post hoc) were performed for the statistically significant differences of SE values per joint DoF and Spearman's rank correlation coefficients of bilateral limbs per phase among those 4 groups. Independent-samples T test and Mann-Whitney U test were performed for the statistically significant differences of SE values and Spearman's rank correlation coefficients per phase between upper and lower limbs for each group. Statistical significance was determined at a p value <0.05. All statistical analyses were performed using IBM SPSS, version 22.0 (SPSS Inc., Chicago, IL, USA).

III. Results

For infants, MDD was relevant to various factors and changed with the increasing biological ages. Although the developmental ages of gross motor were similar among those 4 groups (in this study), the motor development of MDD infants was indeed slower than that of TD infants at the same age. To evaluate the effects of MDD on the inter-joint coordination during infant crawling, we compared the possibly relative differences rather than absolute differences among those 4 groups based on the delayed ages of gross motor.

A. Two Kinematic Synergies Extracted From Joint Angles of Limbs

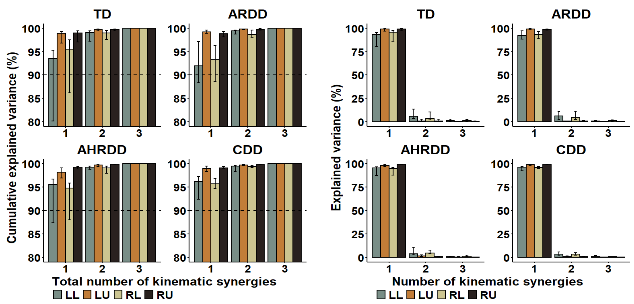
The median, 25th and 75th percentiles of cumulative R^2 values calculated from multi-DoF joint angles using equation (11)

$$\theta_{LSAA} = \arctan\frac{E_y - S_y}{E_z - S_z} \quad (1)$$

$$\theta_{LSFE} = \arctan\frac{E_x - S_x}{E_z - S_z} \quad (2)$$

$$\theta_{LSIR} = \arctan\frac{E_x - S_x}{E_y - S_y} \quad (3)$$

$$\theta_{LEFE} = \arccos\frac{(E_x - S_x)(E_x - W_x) + \left(E_y - S_y\right)\left(E_y - W_y\right) + (E_z - S_z)(E_z - W_z)}{\sqrt{(E_x - S_x)^2 + (E_x - W_x)^2}\sqrt{\left(E_y - S_y\right)^2 + \left(E_y - W_y\right)^2}\sqrt{(E_z - S_z)^2 + (E_z - W_z)^2}} \quad (4)$$



(a) (b)

Fig. 2. (a): Cumulative percentages of explained variance (R^2) from 1 to 3 kinematic synergies (median, 25th and 75th percentiles) for the 4 groups. Dotted lines show the 90% threshold. (b): Percentages of explained variance (R^2) accounted for by each synergy (median, 25th and 75th percentiles) for the 4 groups.

are shown in Fig. 2a. For the four limbs of all infants, the number of kinematic synergies (S) was chosen as 2 according to the selection criteria of synergy number. Thereinto, the first synergy (synergy 1) accounted for at least 70% of the data's variance.

Moreover, the median, 25th and 75th percentiles of R^2 values accounted for by each synergy calculated using equation (8) are shown in Fig. 2b. As shown in this figure, the median of R^2 values for lower limbs were smaller than those for upper limbs, whereas the IQR values of R^2 values for lower limbs were larger than those for upper limbs. The low level of R^2 values accounted for by synergy 3 further indicated that the first two kinematic synergies were sufficient to capture the angular changes of joints per limb during infant crawling.

B. Dynamic Regulation of Kinematic Synergies of Joint Angles for the Crawling Movements

During a crawling cycle, due to similar performances of bilateral limbs for each group, Fig. 3 only shows the median, 25th and 75th percentiles of joint angular profiles for synergy 1 and synergy 2 in LL and LU determined by equation (9) and equation (11). It could be observed that the variation trends of joint angular profiles were similar among those 4 groups. Specifically, for synergy 1, the hip was always adducted during a crawling cycle and reached the maximum adduction at mid-swing. The hip was extended and externally rotated at the beginning, and then flexed and internally rotated at the end of the swing. The hip during stance was mainly moving from the flexed and internally rotated posture to an extended and externally rotated one. The knee was always flexed during a crawling cycle mainly to follow the movement of hip. For synergy 2, the postures of hip and knee were always changed during a crawling cycle. And the variation trends of joint angular profiles for shoulder and elbow were analogous to hip and knee, respectively.

However, for synergy 1 of each group, the knee reached the peak level at the end of the swing, whereas the elbow reached the peak level at mid-swing. Also, the IQR values of HAA, HFE, HIR and KFE were larger than those of SAA, SFE, SIR and EFE respectively, especially in AHRDD and CDD groups. Altogether, the first two kinematic synergies for each group were dynamically regulated during a crawling cycle, and MDD mainly affected the regulation of kinematic synergies for lower limbs during infant crawling.

C. Impact of MDD on the SE Values of Kinematic Synergies of Joint Angles

One-way ANOVA and Kruskal-Wallis one-way ANOVA on ranks showed significant differences of SE values in some joint DoFs among those 4 groups ($p < 0.05$). MDD affected the SE values in some joint DoFs, even if it was not significant according to Bonferroni post hoc test and Tukey post hoc test (see Fig. 4). For synergy 1, the SE values of HIR and EFE during swing and SAA during stance in TD and ARDD groups were smaller than those in AHRDD and CDD groups. For synergy 2, such relationships were observed in KFE during swing and HFE and SFE during stance. No other joint DoFs found such relationships among those 4 groups.

In addition, independent-samples T test and Mann-Whitney U test showed that the SE values of lower limbs were significantly larger than those of upper limbs in: 1) ARDD, AHRDD and CDD groups during swing for synergy 1 (all $p < 0.05$); 2) TD, ARDD and AHRDD groups during swing and AHRDD group during stance for synergy 2 (all $p < 0.05$) (see Table II). No other significant difference of SE values between upper and lower limbs was observed in the 4 groups (all $p > 0.05$). In a word, MDD mainly increased the SE values of joint flexion/extension during infant crawling to some extent, and the SE values of lower limbs were relatively larger than those of upper limbs, especially in AHRDD and CDD groups.

D. Comparison of the Spearman's Rank Correlation Coefficients of Bilateral Limbs

One-way ANOVA and Kruskal-Wallis one-way ANOVA on ranks showed no significant differences of the Spearman's rank correlation coefficients of bilateral limbs for synergy 1 and bilateral upper limbs for synergy 2 per phase among those 4 groups (all $p > 0.05$), but significant differences of bilateral lower limbs for synergy 2 (all $p < 0.05$). Bonferroni post hoc test and Tukey post hoc test further found that for synergy 2, the Spearman's rank correlation coefficients of lower limbs in TD group were significantly smaller than those in AHRDD and CDD groups during swing, but significantly larger than those in ARDD group during stance (all $p < 0.05$) (see Fig. 5).

Besides, independent-samples T test and Mann-Whitney U test showed that the Spearman's rank correlation coefficients of lower limbs were significantly smaller than those of upper limbs for the 4 groups during swing and AHRDD group during stance for synergy 1 (all $p < 0.05$), whereas the opposite relationship was observed in AHRDD group during swing for synergy 2 ($p = 0.024$) (see Fig. 5). No other significant difference between upper and lower limbs was found in the 4 groups (all $p > 0.05$). So, the motor developmental levels of infants did not obviously change the Spearman's rank correlation coefficients of bilateral limbs during crawling, and the Spearman's rank correlation coefficients of bilateral lower limbs were relatively smaller than those of bilateral upper limbs, especially in AHRDD and CDD groups.

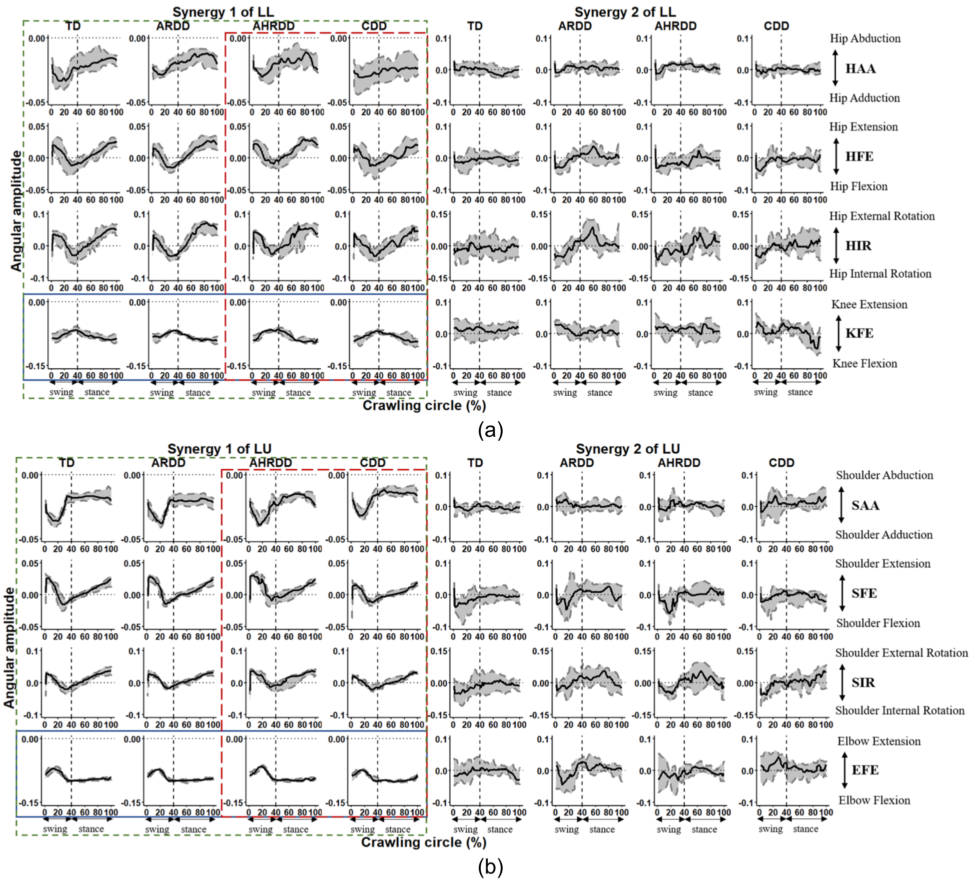


Fig. 3. Joint angular profiles (median, 25th and 75th percentiles) of synergy 1 and synergy 2 in LL and LU during a crawling cycle for the 4 groups. (a): LL. (b): LU. The positive angular amplitudes (y-axis) indicate hip/shoulder abduction/extension/external rotation and knee/elbow extension, whereas the negative amplitudes indicate hip/shoulder adduction/flexion/internal rotation and knee/elbow flexion.

TABLE II
SAMPLE ENTROPY VALUES OF THE FIRST TWO KINEMATIC SYNERGIES OF BILATERAL LIMBS PER PHASE FOR THE 4 GROUPS

Group	Synergy 1						Synergy 2					
	Swing			Stance			Swing			Stance		
	Lower	Upper	p	Lower	Upper	p	Lower	Upper	p	Lower	Upper	p
TD	0.169	0.138	0.104	0.093	0.073	0.152	0.325	0.268	0.006**	0.272	0.252	0.377
	(0.134)	(0.143)		(0.153)	(0.154)		(0.168)	(0.172)		(0.202)	(0.209)	
ARDD	0.163	0.132	0.002**	0.116	0.072	0.113	0.317	0.262	0.006**	0.273	0.280	0.800
	(0.138)	(0.131)		(0.152)	(0.144)		(0.206)	(0.180)		(0.209)	(0.206)	
AHRDD	0.174	0.147	0.029*	0.133	0.091	0.124	0.315	0.300	0.020*	0.334	0.280	0.007**
	(0.147)	(0.159)		(0.145)	(0.168)		(0.202)	(0.173)		(0.226)	(0.170)	
CDD	0.163	0.131	0.019*	0.099	0.091	0.938	0.288	0.300	0.966	0.293	0.292	0.921
	(0.124)	(0.144)		(0.133)	(0.160)		(0.197)	(0.165)		(0.234)	(0.219)	

Data are expressed as median (IQR). The black asterisk represents that the sample entropy values of lower limbs were significantly larger than those of upper limbs. * indicates $p < 0.05$, ** indicates $p < 0.01$.

IV. DISCUSSIONS

The purposes of this study were to explore whether the joint activities of limbs during infant crawling were represented with kinematic synergies of joint angles, and evaluate the effects of MDD on the inter-joint coordination using those synergies. Our results showed that: 1) the first two kinematic synergies sufficiently represented the joint angular profiles of limbs; 2) the development of motor function between upper and lower limbs for infants was asynchronous; 3) MDD further aggravated this asynchronous process and mainly increased the SE values of joint flexion/extension to some extent, but did not obviously change the Spearman's rank correlation coefficients of bilateral limbs.

A. Different Contributions of High- and Low-Order Kinematic Synergies to the Crawling Movements

During infants crawling on hands and knees, the angular changes of joints per limb were manifested as the first two time-varying kinematic synergies, and synergy 1 explained more than 70% of the data's variance (see Fig. 2). Previous studies reported that for arm motion and gait, the multi-order kinematic synergies extracted from the joints and limbs using

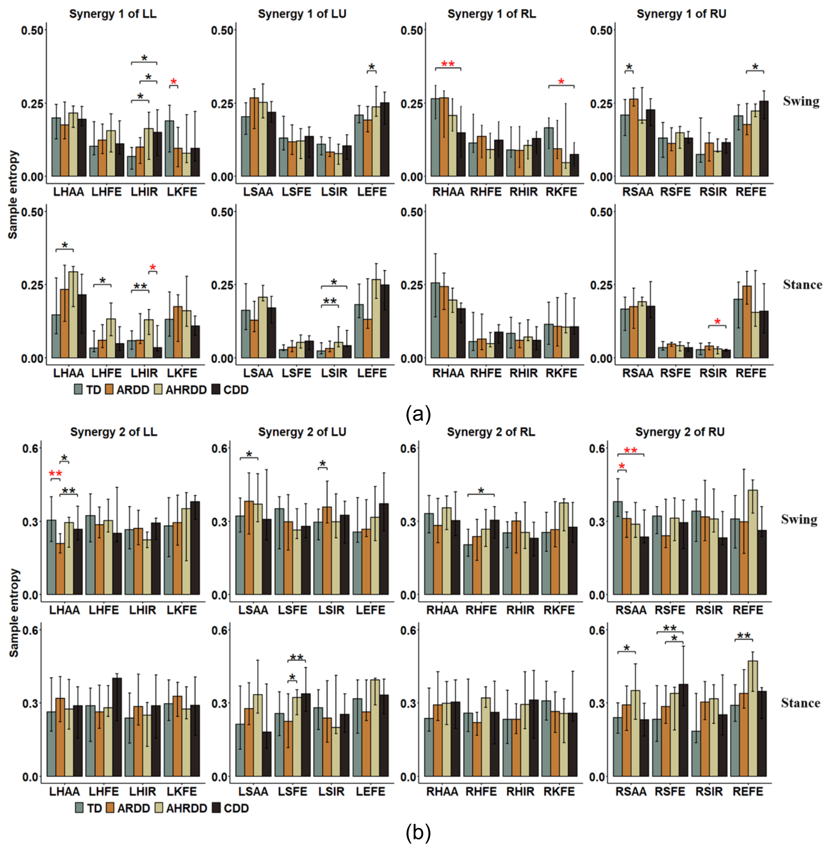


Fig. 4. Sample entropy values (median, 25th and 75th percentiles) per joint DoF of the first two kinematic synergies for the 4 groups. (a): Synergy 1. (b): Synergy 2. The black asterisk represents either relationship of TD < ARDD < AHRDD < CDD, while the red asterisk represents the opposite relationship. * indicates $p < 0.05$, ** indicates $p < 0.01$.

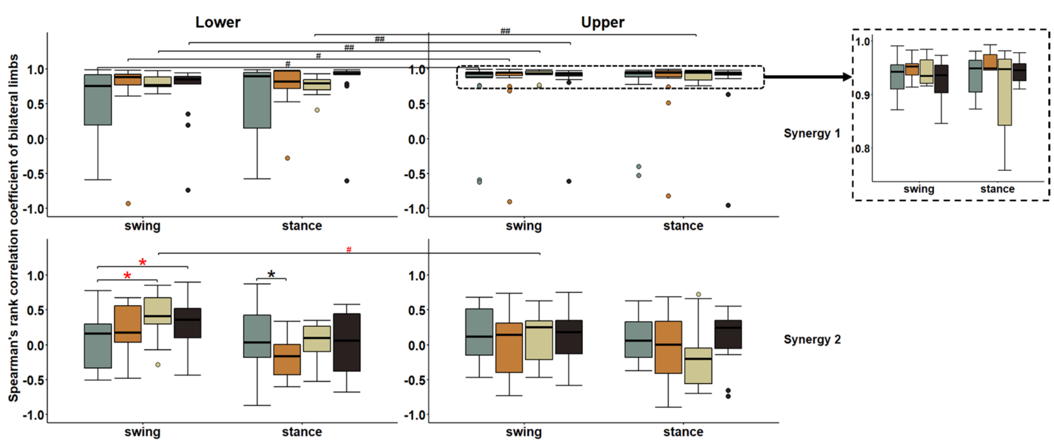


Fig. 5. Spearman's rank correlation coefficients of bilateral limbs based on kinematic synergies of joint angles for the 4 groups. The black asterisk represents either relationship of TD > ARDD > AHRDD > CDD, while the red asterisk represents the opposite relationship. The black pound sign represents that the Spearman's rank correlation coefficients of lower limbs were significantly smaller than those of upper limbs, while the red pound sign represents the opposite relationship. */# indicates $p < 0.05$, **/## indicates $p < 0.01$.

PCA played different physiological roles, where the low-order synergies represented the overall trend of motion patterns, while the high-order synergies fine-tuned the details of motor behaviors [7], [15]. Extending to our results, those multi-order synergies exhibited different contributions to the crawling movements, which was determined by the neuromuscular control strategy of the CNS [9]. Specifically, the low-order synergies (synergy 1) represented the overall trend for limb movement, whereas the high-order synergies (synergy 2) described the adjustment of motor details.

When the limbs of infants alternated in the swing and stance phases successively, their general patterns of the crawling movements were quantitatively similar [14], [22]. As shown in Fig. 3, the major trends of motion patterns (synergy 1), including joint abduction/adduction, flexion/extension, internal/external rotation, were similar among those 4 groups during a crawling cycle so as to allow their limbs to move forward. These results were also observed in most quadruped mammals [16], [33]. Our pilot study also reported that MDD infants could be preliminarily distinguished from TD infants by the first kinematic synergies extracted from the joints and limbs during infant crawling, even if the identification accuracy was not very high [17]. Moreover, due to different levels of the cooperation, learning ability, motion proficiency and environmental factors, human can constantly adjust the details of motor postures in the process of completing a given motion task to balance the energy consumption, movement efficiency and biomechanics [29]. In this study, the above factors affecting the motor postures could be reflected in synergy 2 (Fig. 3), indicating that infants with different motor developmental levels required to make different efforts so as to keep their bodies stable during crawling. Given that infants are inclined to choose the coordinated motion patterns to possibly reduce the bone stresses and the metabolic power [9], [16], those multi-order kinematic synergies with different contributions to the crawling movements provided a new perspective for the development of rehabilitation strategies.

B. Further Delayed Development of Motor Function for Lower Limbs in MDD Infants

The percentages of explained variance for upper limbs in the 4 groups showed higher median and lower IQR values, compared to lower limbs (see Fig. 2b), which indicated better functional control of upper limbs during crawling [31]. That is, the motor commands issued by the CNS can be received faster and execute better by upper limbs than those by lower limbs, validating the top-down rule of the development of body human [19]. These results also agreed to a previous finding, in which Xiong *et al.* observed that the development of motor function for upper limbs was earlier than that for lower limbs in TD infants during crawling [11]. Analogously, this developmental rule can be observed in some quadruped mammals [33]. Our results also observed that the IQR values of lower limbs for joint angular profiles of synergy 1 were higher than those of upper limbs, especially in AHRDD and CDD groups (see Fig. 3). Due to similar delayed ages of gross motor between TD and ARDD groups (see Table I), their motor function would show some similarities. In general, the motor behaviors require multiple joints and limbs to cooperatively participate in the motor control, and the CNS can timely and moderately regulate the joint coordination patterns of limbs to produce purposeful movements [25]. Damage to the CNS, such as in CP [20] or stroke [34], disrupts this regulation process, resulting in further delayed development of motor function for lower limbs. Extending to the hands-and-knees crawling of infants, this points to the importance of motor developmental levels to appropriately recruit the regulation mechanisms of motor function for limbs.

With regards to the crawling complexity (i.e., SE values) (see Table II) and the symmetry of bilateral limbs during crawling (i.e., Spearman's rank correlation coefficients) (see Fig. 5), the movements of lower limbs were also more complex and less symmetrical than those of upper limbs, especially in AHRDD and CDD groups. Previous studies have demonstrated that the abnormal inter-joint coordination of limbs was constrained by a neuromuscular control strategy of the CNS [11], [20], [31]. Therefore, further delayed development of motor function for lower limbs in AHRDD and CDD groups during crawling revealed the impaired motor control caused by the neuromuscular disorders, and this characteristic could also be used as a warning sign of MDD in infant's early life.

C. Mainly Increased Crawling Complexity of Joint Flexion/Extension in MDD Infants

During hands-and-knees crawling, AHRDD and CDD groups mainly showed increased SE values of joint flexion/extension compared to TD and ARDD groups (see Fig. 4). Since the crawling movements required the flexion and extension of joints and limbs to move forward [22], [31], the changes of crawling complexity (i.e., SE values) caused by MDD were mainly reflected in joint flexion/extension. The increased crawling complexity were consistent with the results of motion complexity during walking in CP children, suggesting the impaired motor control of the CNS [28]. In general, the motion complexity during walking showed the trend decreasing with the increasing biological ages from infants to adults, which was related to their biological, cognitive and socio-emotional changes during this period [32]. Previous studies have also demonstrated that the speeds of locomotion changed the joint movement patterns, and human beings chose different joint movement patterns at different speeds to achieve the optimal motion complexity [12], [16], [31]. In the present study, all infants participating in this experiment crawled on hands and knees at their self-selected velocities, which would generate different joint movement patterns. However, MDD affected the sensorimotor interactions and resulted in abnormal descending motor commands, and then produced abnormal joint movement patterns, such as stiff and sluggish joint activities [35]. That is, the CNS chooses the most stable joint movement patterns to keep body safe and avoid the tumble [31], [36], and the additional attention and cortical contribution for MDD infants are required to reduce the motion instability by increasing the crawling complexity.

At the same time, the reduced crawling complexity in ARDD and AHRDD groups or no significant differences of crawling complexity among those 4 groups were also observed in some joint DoFs (see Fig. 4). One possible explanation for those results was the different levels of cognition affecting the understanding of motion tasks [28]. Because MDD infants are at high risk of CP, the cortical motor control may be hindered, being associated with the impaired somatosensory afference from the periphery to the brain [35]. Another possible explanation for those results was the motion proficiency improved with the increasing biological ages for individuals [11], [36]. Obviously, in this study, the biological ages of AHRDD and CDD groups were larger than those of TD and ARDD groups (see Table I). Results in this study suggested that MDD mainly increased the crawling complexity of joint flexion/extension to some extent, even if it was not apparent in all phases.

D. Symmetrical Limb Movement During Crawling in Infant With Different Motor Developmental Levels

Our results demonstrated that the Spearman's rank correlation coefficients of bilateral limbs for synergy 1 were not significantly different among those 4 groups (see Fig. 5), suggesting that similar to TD group, the bilateral limbs of ARDD, AHRDD and CDD groups during crawling also moved symmetrically. A prevailing hypothesis is that the CNS controls the inter-joint coordination patterns so that the bilateral limbs of healthy individuals move symmetrically to produce a smooth and rhythmical motion [36], [37]. However, this hypothesis has not been supported by the observations that individuals with neurological diseases affecting the inter-joint coordination, such as stroke [34], Parkinson's disease [38] and CP [20], have the asymmetrical movement of bilateral lower limbs. In this study, the increased crawling complexity of joint flexion/extension (see Fig. 4) also reduced the symmetry of bilateral limbs for MDD infants during crawling to some extent, and then resulted in the similar symmetry of bilateral limbs among those 4 groups. From the previous studies, the impairments of the CNS for CP destroyed the regulation mechanisms of motor function, but were unable to obviously change the symmetry of bilateral limbs in CP children during crawling [12]. In contrast, the increased symmetry of bilateral lower limbs during swing for synergy 2 in AHRDD and CDD infants (see Fig. 5) was relevant to the improvement of motion proficiency with the increasing biological ages [11]. In addition, it has been suggested that the limb movement was the results of the integration of biomechanics, neurophysiology and motor control, so these asymmetrical behaviors of bilateral limbs reflected the natural functional differences rather than the abnormalities [37]. Our results indicated that the difference of the symmetry of bilateral lower limbs during stance for synergy 2 between TD and ARDD groups (see Fig. 5) could also emerge as the results of natural function differences, which was affected by different motor control strategies [10].

Some negative or extremely low Spearman's rank correlation coefficients of bilateral limbs were also observed in the 4 groups during crawling (see Fig. 5). Those negative coefficients might be related to the abnormal muscle control and different levels of muscle contractions in different sides, while those extremely low coefficients might be related to the motor balance disorders, motor incoordination and other factors [12], [36], [37]. Considering the above results, we speculated that the symmetrical movements of bilateral limbs for MDD infants during crawling appeared to be a compensation mechanism of motor function, which could minimize the bilateral asymmetry of MDD, and even make bilateral symmetry [20], [28], [36].

V. Conclusion

To our knowledge, this paper is the first one to evaluate the effects of MDD on the inter-joint coordination during infant crawling under the perspective of kinematic synergies of joint angles. The present results reveal that the first two kinematic synergies with different contributions to the crawling movements sufficiently represent the joint angular profiles of limbs. During infants crawling on hands and knees, MDD further delays the development of motor function for lower limbs and mainly increases the crawling complexity of joint flexion/extension to some extent, but does not obviously change the symmetry of bilateral limbs. The main limitation is the restriction of the study to a limb, while the crawling movements require multiple limbs to cooperatively participate in the motor control.

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