

Kinematic-muscular synergies describe coupled neuro-muscular control and biomechanics of locomotion in children with cerebral palsy

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ABSTRACT

In children with cerebral palsy (CP), gait impairments originate from altered neuromuscular control and result in abnormal biomechanical outcomes. Muscle synergy analysis has been used to investigate modular motor control, but it relies exclusively on electromyographic (EMG) data. Kinematic-muscular synergies integrate EMG signals and kinematic variables, associating the neural commands with the biomechanics of the movement. This study examined kinematic-muscular synergies during gait in children with CP to identify alterations in both synergy structure and temporal activation. Seventeen children with CP were stratified based on their age (children, adolescents, and young adults). Twenty-two typically developed (TD) children served as the reference. Mixed-matrix factorization was used to extract kinematic-muscular synergies from 8 lower limb muscles and four joint accelerations in the sagittal plane. Spatial synergy structures were more consistent in TD and children than in adolescents ($p = 0.04$) and young adults ($p = 0.001$), while consistency of temporal coefficients was higher in TD ($p < 0.001$). Comparisons of patients with TD children revealed generally moderate preservation of spatial synergy structure, but temporal recruitment patterns diverged with age. Kinematic-muscular synergy analysis provides a quantitative link between impaired muscle coordination and altered biomechanics in CP gait, offering a promising tool for enhanced gait assessment and personalized rehabilitation planning.

1. Introduction

Cerebral Palsy (CP) is a group of permanent, non-progressive motor and postural disorders caused by lesions or malformations in the developing brain (Tang et al., 2019). It is one of the most prevalent motor disabilities in childhood (Patel et al., 2024), commonly associated with impaired motor control, abnormal muscle tone, and coordination deficits that often persist throughout life. Functional severity is commonly evaluated with the Gross Motor Function Classification System (GMFCS) (Palisano et al., 1997), which categorizes individuals into five levels according to self-initiated mobility and reliance on assistive devices (Rosenbaum et al., 2007; Wood and Rosenbaum, 2000). Another scale used for CP children is the Functional Mobility Scale (FMS), which classifies the functional mobility taking into account the assistive

devices a child might use for covering 5 m, 50 m, and 500 m (Graham et al., 2004). These frameworks allow clinicians and researchers to describe motor performance, stratify cohorts, and compare outcomes across studies.

Overground walking develops throughout childhood, reflecting the maturation of neuromuscular control and postural coordination (Dominici et al., 2011; Ivanenko et al., 2013). In typically developed (TD) children, gait patterns evolve from variable, co-contracted patterns to more stable and efficient coordination (Xiong et al., 2022). Understanding how gait pattern develops through age in people with CP is crucial to identify deviations from typical maturation, providing insight into compensatory mechanisms and residual motor control capacity.

During tasks such as postural control and walking, electromyographic (EMG) analyses have revealed abnormalities in CP, including

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altered activation timing and excessive antagonist co-contraction (Steele et al., 2015). Muscle synergy analysis has been widely used to investigate motor control, which suggests that the central nervous system (CNS) simplifies motor control by activating a limited set of spatial and/or temporal patterns (Bizzi et al., 2008), or muscle synergies, extracted from EMG signals. In locomotion, studies converge on the existence of four to five synergies associated with key biomechanical functions (Chia Bejarano et al., 2017; Ghislieri et al., 2020; Ivanenko et al., 2004; Rimini et al., 2017), including weight acceptance, propulsion, swing initiation, and limb deceleration. In addition, these modules seem to be robust across individuals and walking conditions (Chvatal and Ting, 2013), such as changes in walking speed (Marino et al., 2024; Rimini et al., 2017), body weight support (Ivanenko et al., 2004), or shift from walking to running (Cappellini et al., 2006). In contrast, pathological control is marked by a general reduction in the number of synergies, proportional to impairment severity (Bowden et al., 2010). Indeed, children with CP often recruit fewer synergies during walking compared to TD children, suggesting reduced motor complexity (Bekius et al., 2020; Beltrame et al., 2023; Steele et al., 2019). Moreover, children with CP demonstrate altered synergy structure and increased stride-to-stride variability of synergies compared to TD children (Kim et al., 2018; Shuman et al., 2016).

Conventional synergy analyses rely solely on EMG signals, limiting the direct interpretation of biomechanical outcomes. A promising approach is the kinematic-muscular synergy model, which integrates EMG activation patterns and kinematic variables within the same modular framework (Scano et al., 2022). This hybrid method directly links muscle coordination to kinematic execution, strengthening the interpretation of motor modules in functional biomechanical terms. Kinematic-muscular synergies have been shown to effectively describe locomotor biomechanics in healthy adults (Lanzani et al., 2024). Although applications in patient populations have yet to be analyzed, kinematic-muscular synergy analysis has the potential to reveal impairments in motor coordination and compensatory strategies in children with CP. Most previous studies have compared children with CP to TD peers, often without considering the age-related changes within the CP population. Therefore, to reduce age-related confounding effects, participants with CP were grouped by age, allowing the investigation of how motor control strategies evolve across maturation within the CP population. In fact, motor control and gait patterns in CP may continue to evolve beyond childhood, influenced by maturation, therapy, and compensatory mechanisms (Johnson et al., 1997). Investigating how muscle coordination changes across age in CP can therefore offer insight into the developmental trajectory of neuromuscular control. Accordingly, the aim of this study was to examine kinematic-muscular synergies during gait in TD children and in individuals with CP across age groups. We hypothesized that individuals with CP would show age-dependent changes in the composition and temporal activation of synergies, reflecting ongoing adaptation of motor control strategies.

2. Materials and methods

2.1. Participants

Seventeen children with Cerebral Palsy (11 M, 6F; age: 13.3 ± 3.8 years old, weight: 49.0 ± 16.3 kg, height: 154.0 ± 16.7 cm), were recruited for the study. The normative group consisted of twenty-two typically developed (TD) male children (age: 9.0 ± 1.4 years old, weight: 30.3 ± 7.5 kg, height: 134.5 ± 10.2 cm), with no history of musculoskeletal disorders. Children with pain, traumatic injuries, or any musculoskeletal or neurological conditions were excluded.

This study was conducted at the Movement Analysis Laboratory of the Humanitas Research Hospital (Rozzano, Milano, Italy), in collaboration with the Italian Council of National Research (CNR, Milan, Italy). Written informed consent was obtained from all participants before participation. The study protocol complied with the principles of the

Declaration of Helsinki and was reviewed and approved by the Humanitas Ethical Committee.

2.2. Experimental protocol

Participants underwent a single evaluation session that included three-dimensional gait analysis. Each subject was asked to walk barefoot along a 5-m walkway at a self-selected comfortable speed. Kinematic data were recorded using an 8-camera optoelectronic motion capture system (Vicon 8 TVC system, Oxford, UK), synchronized with a 45x50cm force platform (AMTI 100 MHz, Advanced Medical Technologies, Watertown, Massachusetts). Before the trials, anthropometric measurements were collected. Sixteen reflective markers were placed on anatomical landmarks according to the Helen Hayes marker set, implemented in the Vicon Plug-in-Gait (PiG) model. Markers were positioned on the anterosuperior and posterior-superior iliac spines, 1/3 of the lower lateral surface of the thigh, the lateral femoral epicondyle, 1/3 of the proximal tibia, the lateral malleolus, the head of the second metatarsal, and the calcaneus.

Surface EMG was recorded using 16 bipolar electrodes (Cometa, Italy), with eight placed on each side. Electrodes were placed over the muscle belly, aligned with the muscle fiber direction, following the SENIAM recommendations when available (Hermens et al., 2000). The electrode positions were identified by palpation and by visual inspection of the contracting muscles. Before placement of the electrodes, the surface of the skin over the muscles of interest was shaved and rubbed with an alcohol-damp swab in order to remove dirt, sweat, and dead skin. Electrodes were circular (radius 8 mm), and the center-to-center electrode distance was 20 mm. The following muscles were recorded: Tibialis Anterior (TA), Gastrocnemius Lateralis (GL), Gastrocnemius Medialis (GM), Rectus Femoris (RF), Semitendinosus (ST), Biceps Femoris (BF), Adductor Magnus (ADD), and Gluteus Maximus (GI). EMG data were synchronized with the kinematic recordings and acquired simultaneously. All assessments were performed by the same two physiotherapists, both experienced in gait analysis, to ensure consistency.

2.3. Data analysis

Raw marker trajectories were low-pass filtered at 6 Hz, while force platform signals were filtered at 40 Hz using a fourth-order, phase-corrected Butterworth filter. The gait cycle was defined as the interval between two consecutive heel strikes of the same foot. The Heel-Strike events were first identified from the force plate data and then confirmed using the Vicon autocorrelation pipeline, followed by visual inspection of the vertical displacement of the heel marker (Fellin et al., 2010). Spatiotemporal parameters such as cadence (steps/min), walking speed (m/s), stride time (s), stride length (m), and foot off (% gait cycle) were computed. Spatiotemporal parameters were averaged across all recorded gait cycles from both limbs. For hemiparetic participants, this includes both paretic and non-paretic strides. This aggregated approach was chosen to provide a representative, macroscopic overview of the cohort's global walking performance, preventing excessive data fragmentation that would result from separating limb-specific parameters across the diverse clinical subtypes included in the study. Pelvis, hip, knee, and ankle kinematics in the sagittal plane were low-pass filtered at 6 Hz and resampled to 101 points per stride. Angular accelerations of these joints were calculated as the second derivative of the corresponding joint angles. Each acceleration profile was normalized to the maximum absolute value (range: -1 to 1) and resampled to 101 points per stride. Acceleration was chosen as it better reflects dynamic demands rather than posture, and couples in a reasonably linear way with EMG (force).

For EMG analysis, bilateral EMG signals were collected at 2000 Hz, band-pass filtered between 20 and 450 Hz, rectified, and then low-pass filtered at 10 Hz to generate envelopes (d'Avella et al., 2006). To enable

inter-subject comparison, EMG envelopes were normalized to the peak activation of each muscle and resampled to 101 points per stride. For each participant, the filtered and normalized EMG envelopes were combined with the joint angular accelerations to create pooled matrices for input into the synergy extraction algorithm. Approximately ten gait cycles were recorded for each participant, and the cycles affected by artifacts or noise were excluded. A mean of 9.1 ± 1.9 gait cycles was used for TD participants, and a mean of 8.8 ± 4.3 gait cycles was used for patients. Kinematic and EMG data were processed bilaterally. Synergies were extracted independently for each limb (left and right), resulting in a total pool of 44 limbs for TD participants and 34 limbs for patients, analyzed as separate observations to account for the potential pathological asymmetries.

2.4. Synergy extraction and clustering

Synergy extraction methods decompose the multichannel input signals $x(t)$ into the product of n time-invariant synergy vectors w_i , which are shared across all stride repetitions, and corresponding time-varying activation coefficients $c_i(t)$, which are stride-specific:

$$x(t) = \sum_{i=1}^N c_i(t) w_i$$

Here, $x(t)$ represents the recorded kinematic and muscular data at time t , and N is the total number of extracted synergies. Kinematic-muscular synergies were extracted using the mixed-matrix factorization (MMF) algorithm (Russo et al., 2024; Scano et al., 2022), an extension of the widely used non-negative matrix factorization (NMF) approach (Lee and Seung, 1999). Unlike NMF, MMF removes the non-negative constraint for selected channels (joint accelerations, which can assume positive or negative values). The algorithm iteratively decomposes $x(t)$ via gradient descent, with setup parameters $\lambda = 100$ and $\mu = 0.1$, empirically tuned to balance reconstruction accuracy and computational efficiency (Scano et al., 2022).

The number of synergies, s , was increased from 1 to 12 (maximum channels per leg). For each s , MMF was repeated 100 times to avoid local minima, and the solution explaining the variance was selected. Reconstruction accuracy was assessed by $R^2 = 1 - SSE/SST$, where SSE is the sum of the squared residuals, and SST is the total sum of squares relative to the mean EMG vector (d'Avella et al., 2006). The final number of synergies N was defined as the minimum number of modules required to account for at least 85% of the signal variance ($R^2 > 0.85$). This threshold was selected to balance reconstruction accuracy with model parsimony, preventing the over-factorization of noise-driven components often observed in clinical data. This criterion provides a consistent and reproducible evaluation across participants and aligns with previous synergy literature (Barroso et al., 2016; Lanzani et al., 2024).

Since TD participants fell within a relatively narrow age range, they were treated as a single reference cohort representative of physiological motor coordination patterns within the investigated developmental stage. In contrast, the CP cohort spanned a substantially broader age range and exhibited greater inter-subject variability, making stratification necessary to specifically investigate maturation-related changes in pathological motor control. Patients were divided by age into (1) *CP children* (6 to 11 years), (2) *CP adolescents* (12 to 15 years), and (3) *CP young adults* (16 to 20 years). For each group of participants, spatial synergies were matched based on cosine similarity. Pairwise similarity between synergies was computed, and synergies with the highest similarity were clustered together. The maximum number of clusters was set equal to the maximum number of synergies extracted from each participant. For each cluster, a representative synergy was obtained by averaging the spatial patterns of all included synergies.

2.5. Outcome measures and statistics

To compare differences in motor control dimensionality across

groups, the number of synergies extracted at the reconstruction threshold of $R^2 > 0.85$ (Barroso et al., 2016; Lanzani et al., 2024) was assessed. Since the data did not satisfy the normality assumption, the non-parametric Kruskal-Wallis test was applied, followed by a post-hoc test with Bonferroni correction for multiple comparisons across the different groups. Intra-cluster similarity of spatial synergies was quantified using the scalar product between all pairs of synergies within each cluster, while intra-cluster similarity of temporal coefficients was computed using Pearson's correlation coefficient between all corresponding pairs of temporal profiles. These measures provide indices of synergy consistency within each group. Group differences in both spatial and temporal intra-cluster similarities were evaluated using the Kruskal-Wallis test, followed by Bonferroni-corrected post-hoc comparison. Statistical significance was set at $\alpha = 0.05$ for all analyses.

To evaluate whether the synergy structure and timing were preserved in patient groups, clusters derived from each patient group were matched to those from the TD group. Inter-cluster similarity was computed as the scalar product between matched mean spatial synergies, and inter-cluster temporal similarity was quantified as the correlation coefficient between matched mean temporal profiles. These inter-cluster metrics characterize the extent to which synergy composition and temporal organization are maintained in patients with respect to the normative group. To better assess the differences in the temporal profiles across groups, circular cross-correlation was computed (Frère and Hug, 2012; Kaufmann et al., 2024). The maximum cross-correlation ($r_{\max}$) was used as a measure of similarity in the shape of the temporal coefficients, whereas the corresponding lag (Lag%) was used to quantify temporal alignment between signals. The shift was expressed as a percentage of the total cycle duration, allowing interpretation of timing differences, with positive values indicating a delayed (lagged) signal and negative values indicating an earlier (advanced) signal.

3. Results

3.1. Clinical outcomes

Table 1 summarizes patients' data and clinical scales (GMFCS, FMS 50 m, and FMS 500 m). In the table, the clinical diagnosis of the gait pattern of the groups is reported. The age difference between groups is statistically significant ($p < 0.005$).

3.2. Kinematics

The number of children in each group was: five in the CP children group, seven in the CP adolescent group, and five in the CP young adults group. In Fig. 1, joint angles of pelvis, hip, knee, and ankle in the sagittal plane are shown as averages for each of the groups.

Articular angle trajectories in the TD group exhibit typical gait patterns and demonstrate high consistency across participants, with slight variability only in the pelvis orientation. For participants with CP, Children display increased anterior pelvic tilt, reduced hip extension, and a diminished knee and ankle range of motion. CP Adolescents present greater variability in kinematic profiles, characterized by less ankle plantarflexion. CP Young adults show higher pelvic range of motion, but less movement in the other joints. All patient groups show greater variability with respect to TD children.

In Table 2, spatiotemporal parameters are reported. The cadence of CP adolescents and CP young adults was lower than that of TD ($p < 0.001$) and CP children ($p = 0.004$, $p = 0.005$). TD children walked faster than all patients ($p < 0.001$). The stride time was lower for TD children than for all patients ($p < 0.001$), and for CP children than for CP adolescents ($p = 0.006$) and CP young adults ($p = 0.02$). The stride length was greater for TD children than for all patients ($p < 0.001$) and was lower for CP children than for CP adolescents ($p < 0.001$) and CP young adults ($p < 0.001$). The foot off was lower for TD than for all the patients

Table 1

Patients' personal data and clinical scales. Clinical diagnosis is reported for descriptive purposes only and was not used for subgroup stratification due to the uneven age distribution across diagnostic categories.

CP Children					
ID	age	GMFCS	FMS 50 m	FMS 500 m	Diagnosis
01	6	2	4	2	Spastic diplegia, bilateral valgus condition
02	7	1	6	5	Left hemiparesis
03	8	2	4	2	Right hemiparesis
04	11	2	4	2	Lower-limb deformity and bilateral equinus
05	11	1	6	5	Right hemiparesis
	8.6 (2.3)	1.6 (0.5)	4.8 (1.1)	3.2 (1.6)	
CP Adolescents					
ID	age	GMFCS	FMS 50 m	FMS 500 m	Diagnosis
06	13	1	6	5	Spastic diplegia
07	13	2	4	2	Spastic diplegia
08	13	2	4	2	No definitive diagnosis
09	13	2	4	2	Spastic diplegia, crouch gait
10	14	1	6	5	Spastic diplegia
11	15	3	2	1	Spastic diplegia
12	15	1	6	5	Spastic diplegia
	13.7 (0.9)	1.7 (0.8)	4.6 (1.5)	3.1 (1.8)	
CP Young adults					
ID	age	GMFCS	FMS 50 m	FMS 500 m	Diagnosis
13	16	2	4	2	Lameness, gait with a dragging foot
14	16	1	6	5	Spastic diplegia, intra-rotation of the left femur
15	17	2	4	2	Spastic diplegia, bilateral equinus condition
16	18	1	6	5	Spastic diplegia
17	20	2	4	2	Spastic diplegia, equinus, adductor retraction
	17.4 (1.7)	1.6 (0.5)	4.8 (1.1)	3.2 (1.6)	

($p < 0.001$).

3.3. Synergy analysis

In Fig. 2, the reconstruction R^2 of TD participants and all patient groups is shown. The number of synergies extracted at $R^2 > 0.85$ was 5.4 (0.5) in the TD group, 5.0(0.7) in the CP children group, 4.9(0.7) in the CP adolescents group, and 5.0(0.5) in the CP young adults group.

Figs. 3 and 4 present the clustered synergies and their corresponding temporal coefficients for all groups. W1 reflects hip and knee extension during early stance, driven by gluteus activation together with RF, while ST and BF contribute to knee stability through co-activation. Patients preserved joint kinematics but showed altered muscle recruitment, with reduced gluteus activation and greater variability in temporal coefficients. W2 corresponds to late stance propulsion, with gastrocnemii activation and ankle plantarflexion. Structure was preserved in CP children, while CP adolescents and CP young adults showed increased co-contraction and progressive divergence in temporal patterns. W3 marks the early swing with hip and knee flexion. All groups of patients maintained kinematic loads of the hip and knee joints only, but they showed changes in the ankle joint and exhibited marked co-activation of all muscles. Additionally, CP young adults showed reduced temporal

modulation. W4 involves knee extension and ankle dorsiflexion during mid-swing and was the most similar synergy between patients and TD, except for CP young adults, who did not match the activation of RF and ADD. W5 reflects late swing knee flexion driven mainly by kinematics and TA; patients showed additional hip and knee extensor recruitment and reduced temporal modulation. W6 represents stride preparation (TA, ST, BF activation) and diverged in patients, with altered recruitment and absence of a clear late-swing activation peak.

In Table 3, intra-cluster and inter-cluster similarities of synergy and temporal coefficients are reported. Consistency of spatial synergies was highest in the TD group, with a mean intra-cluster similarity of 0.68. Similarly, temporal recruitment patterns showed the highest consistency in the TD group, with a mean intra-cluster correlation of 0.68. Spatial intra-cluster similarity of the TD group was higher than all patient groups ($p < 0.001$), and the similarity of the CP children group was higher than CP adolescents ($p = 0.04$) and CP young adults ($p = 0.001$). Temporal coefficients intra-cluster correlation of the TD group was higher than all patient groups ($p < 0.001$). Comparisons of patients with TD children (inter-cluster similarity) revealed generally moderate preservation of spatial synergy structure, except W6, which showed the worst similarity. Temporal recruitment patterns were maintained better in the CP children group, while they became more different with age, as shown by the inter-cluster correlation. In this case, C5 is the least preserved temporal coefficient. When comparing the shape of temporal coefficients between patients and TD participants, CP children showed the lowest correlation in C5 and C6, whereas CP young adults exhibited the lowest correlation in C3. Regarding temporal alignment, C5 in CP children and C6 in CP adolescents were delayed relative to TD, while C3 in CP young adults showed an anticipatory shift.

In Fig. 5, the color maps represent the similarity of spatial synergies and the correlation of temporal coefficients of each synergy for all pairwise comparisons between groups. The mean random similarity, computed by randomly pairing all spatial synergies, is 0.23(0.37). The mean random correlation, computed by randomly correlating all temporal coefficients, is 0.02(0.45). Across all synergies, similarity values range from low to moderate. Higher similarity values are generally observed in comparisons involving TD and CP children, while lower values are found in comparisons involving CP young adults. Among spatial synergies, W6 shows the lowest similarity values across most group comparisons. The mean similarity across all spatial synergies indicates higher mean similarity for CP children compared with CP adolescents and CP young adults. Correlation values are moderate to high across most comparisons. Higher correlations are observed between TD and CP children and between CP adolescents and CP young adults, whereas lower correlations appear in comparisons between CP children and CP young adults. Among the temporal coefficients, C5 and C6 show lower correlation values compared with the other coefficients. C5 shows the highest values, exceeding 0.80 in all the comparisons. The mean correlation values confirm these trends across coefficients. Considering the shape of the temporal coefficients, C4 showed the highest similarity across all comparisons, together with relatively small shifts. CP young adults exhibited the lowest similarity for C3 compared with all other groups, whereas CP children showed the lowest similarity for C5 relative to TD participants. Regarding temporal alignment, CP young adults displayed an anticipatory pattern in C3 with respect to TD, as well as in C1 and C6 when compared to CP adolescents. In contrast, CP children showed a delayed pattern in C5 relative to TD, while CP adolescents exhibited a delay in C6 with respect to TD.

4. Discussion

4.1. Summary of the results

In this study, gait patterns were assessed in TD children and in children with cerebral palsy by means of the novel kinematic-muscular synergy analysis. Children with CP were divided into subgroups

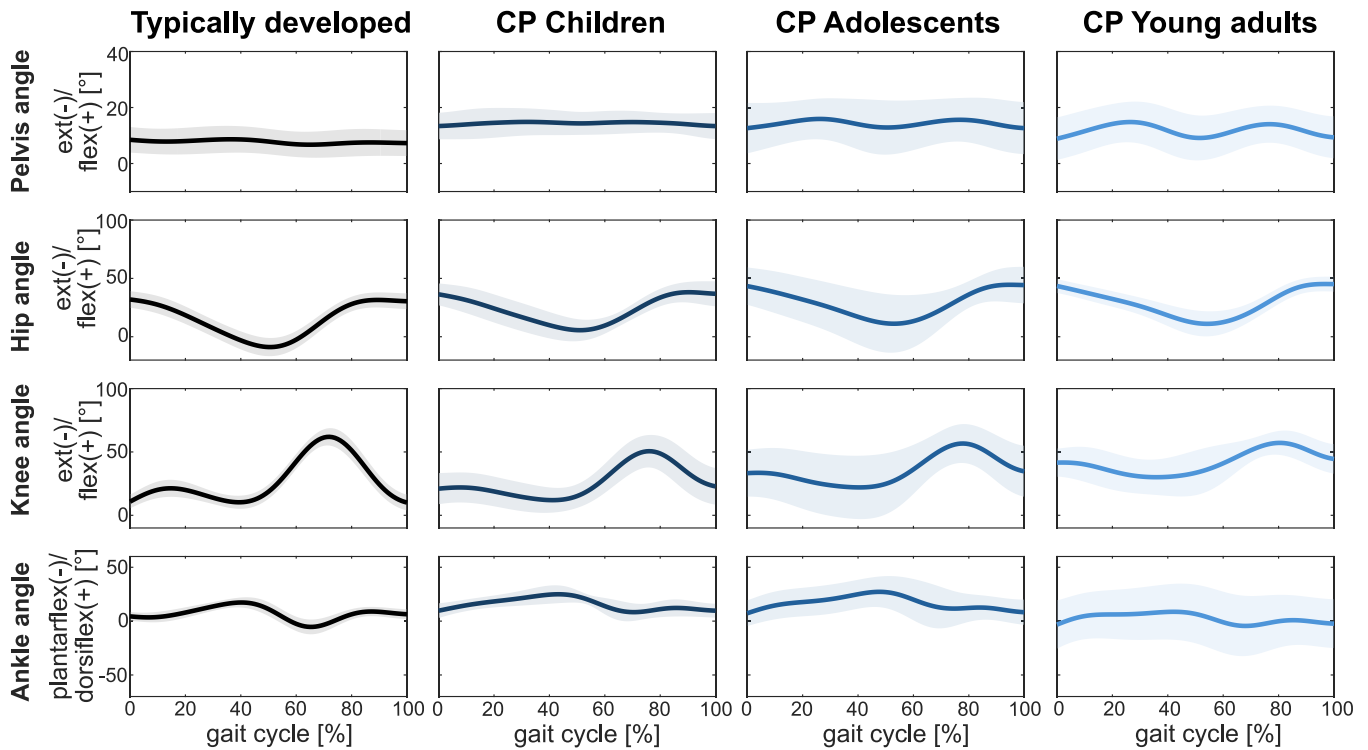


Fig. 1. Sagittal plane angular kinematics. Pelvis, hip, knee, and ankle angles during the gait cycle are reported in the rows, and groups (TD, CP children, CP adolescents, and CP young adults) are reported in columns. Thick lines represent the mean values across participants, and shaded areas represent the standard deviation.

Table 2

Spatiotemporal parameters are reported for each group as mean and standard deviation (in brackets). Parameters were averaged across all recorded gait cycles from both limbs. For hemiparetic participants, this includes both paretic and non-paretic strides.

Parameter	TD	CP children	CP adolescents	CP young adults
Cadence (steps/min)	119.2 (13.7)	114.7 (27.2)	101.9 (14.5)* [^]	101.6 (10.9)* [^]
Walking speed (m/s)	1.08 (0.18)	0.65 (0.24)*	0.71 (0.24)*	0.66 (0.13)*
Stride time (s)	1.01 (0.13)	1.11 (0.36)*	1.20 (0.22)* [^]	1.20 (0.15)* [^]
Stride length (m)	1.07 (0.15)	0.65 (0.18)*	0.81 (0.20)* [^]	0.76 (0.14)* [^]
Foot off (%)	58.4 (3.3)	63.9 (6.5)*	65.1 (7.3)*	65.7 (7.2)*

* p significant when compared to TD; [^] p significant when compared to CP children.

according to their age in order to investigate the alteration of motor strategies during maturation. From a spatiotemporal perspective, TD children exhibited faster walking speed, longer stride length, and shorter stride time compared with all patient groups, reflecting a more efficient gait. In contrast, CP adolescents and CP young adults showed reduced cadence and slower gait, suggesting a progressive shift toward slower and more cautious walking strategies with age. Spatial synergy structures demonstrated moderate intra-group consistency across all cohorts. Temporal recruitment profiles exhibited higher variability in children with CP. When comparing patient groups with TD children, spatial synergies appeared moderately preserved, although with greater muscular co-activation. Temporal synergy profiles, instead, showed substantial deviations in the timing of muscle activation in the swing phase. Kinematic-muscle synergies integrate muscle activity with joint-level biomechanical output. Our approach allows to distinguish between preserved kinematic patterns and altered muscle recruitment, identify how abnormal muscle coordination translates into specific kinematic deviations, and capture both structural and temporal alterations, including changes in activation timing and phase shift.

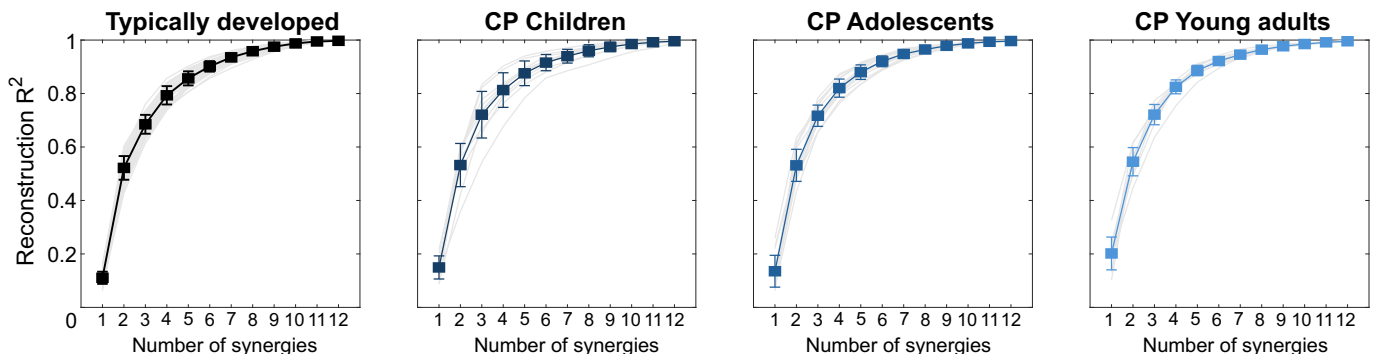


Fig. 2. Mean and standard deviation of the reconstruction R^2 across participants of each.

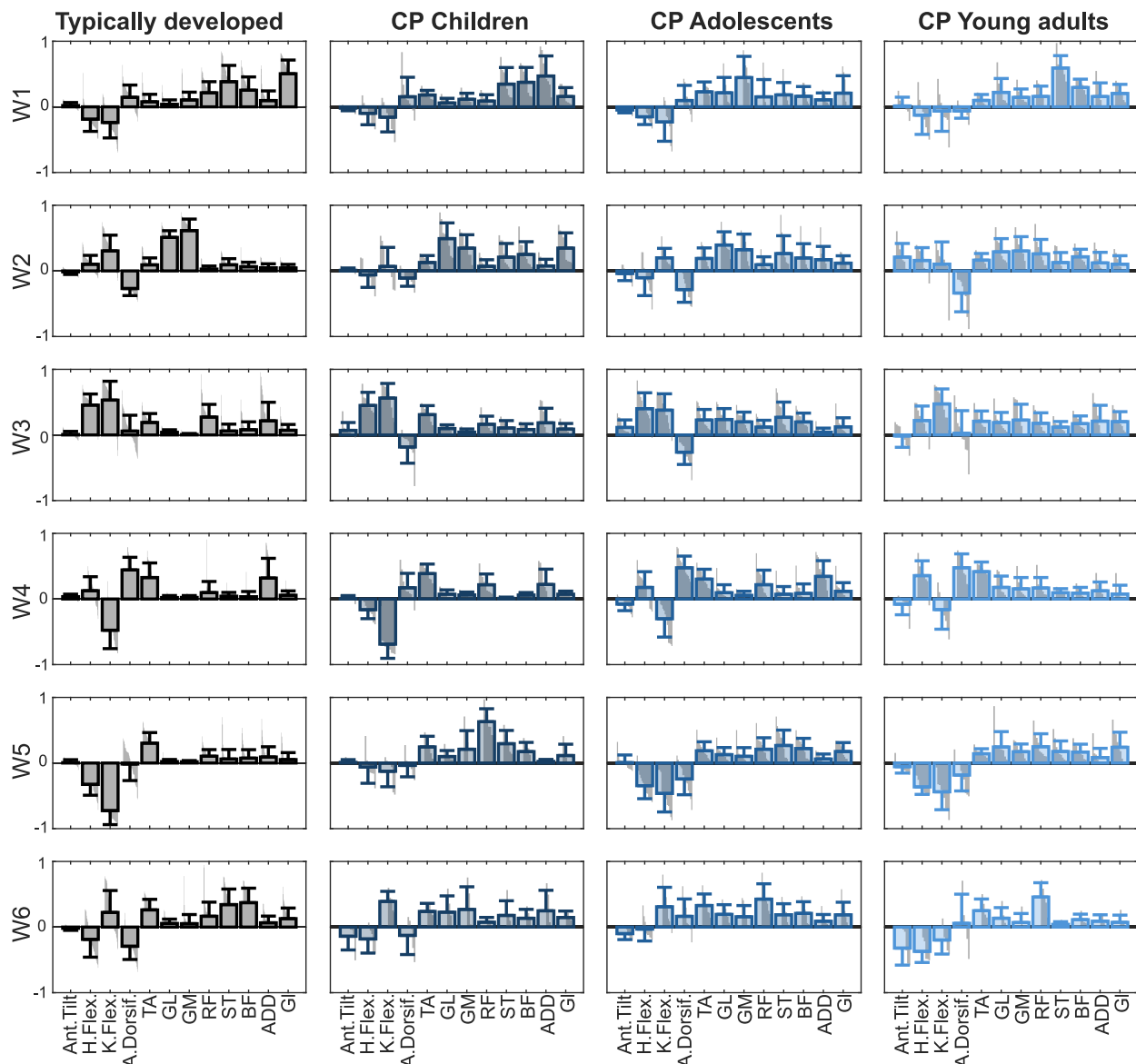


Fig. 3. Synergy compositions of all groups are reported in columns (TD in black, CP children in dark blue, CP adolescents in blue, and CP young adults in light blue). Bold bars are the mean synergy of the cluster, while the grey bars represent all the synergies belonging to the cluster. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

4.2. Kinematic-muscular synergies reflect the biomechanics in patients

Kinematic-muscular synergies describe both muscle coordination and its biomechanical role. In the TD group, synergies are well-defined, showing selective muscle recruitment and consistent temporal activation. Each module corresponded to a specific biomechanical function: W1 supported the early stance through the hip extension; W2 generated plantarflexor-driven propulsion in late stance; W3 coordinated hip and knee flexion at swing onset; W4 controlled mid-swing dorsiflexion and knee extension for toe clearance; W5 mainly reflected inertial limb advancement and TA activation; and W6 prepared foot placement for the next stride.

Across all CP groups, the overall spatial structure was moderately preserved. However, this was accompanied by increased muscle co-activation, particularly in CP adolescents and CP young adults, indicating reduced motor selectivity. This was especially evident in swing-related synergies (W3 and W4), where these groups of patients exhibited simultaneous activation of multiple muscle groups despite relatively preserved joint kinematics. An interesting result is the dissociation

between spatial structure and temporal organization. While spatial modules remained relatively stable across groups, temporal coefficients showed substantial alterations, including reduced modulation, increased variability, and phase shifts. These alterations were particularly evident in late swing synergies (W5 and W6), which showed the lowest inter-group correlation and the greatest deviations in temporal recruitment in all groups. The analysis of temporal alignment revealed that differences between groups were not limited to waveform shape but also involved time shifts. For example, delays were observed in C5 in CP children and in C6 in CP adolescents, whereas CP young adults exhibited anticipatory activation in C3. These findings suggest that impaired motor control in CP is not only characterized by altered activation patterns but also by misalignment in the timing of muscle recruitment within the gait cycle. Among all modules, W4 emerged as the most preserved synergy across groups, both in structure and timing, suggesting that mid-swing control for toe-clearance may be relatively robust to pathology. In contrast, W6 showed the lowest similarity and the greatest temporal disruption, indicating that late swing preparation is particularly vulnerable in CP. Overall, CP children showed patterns

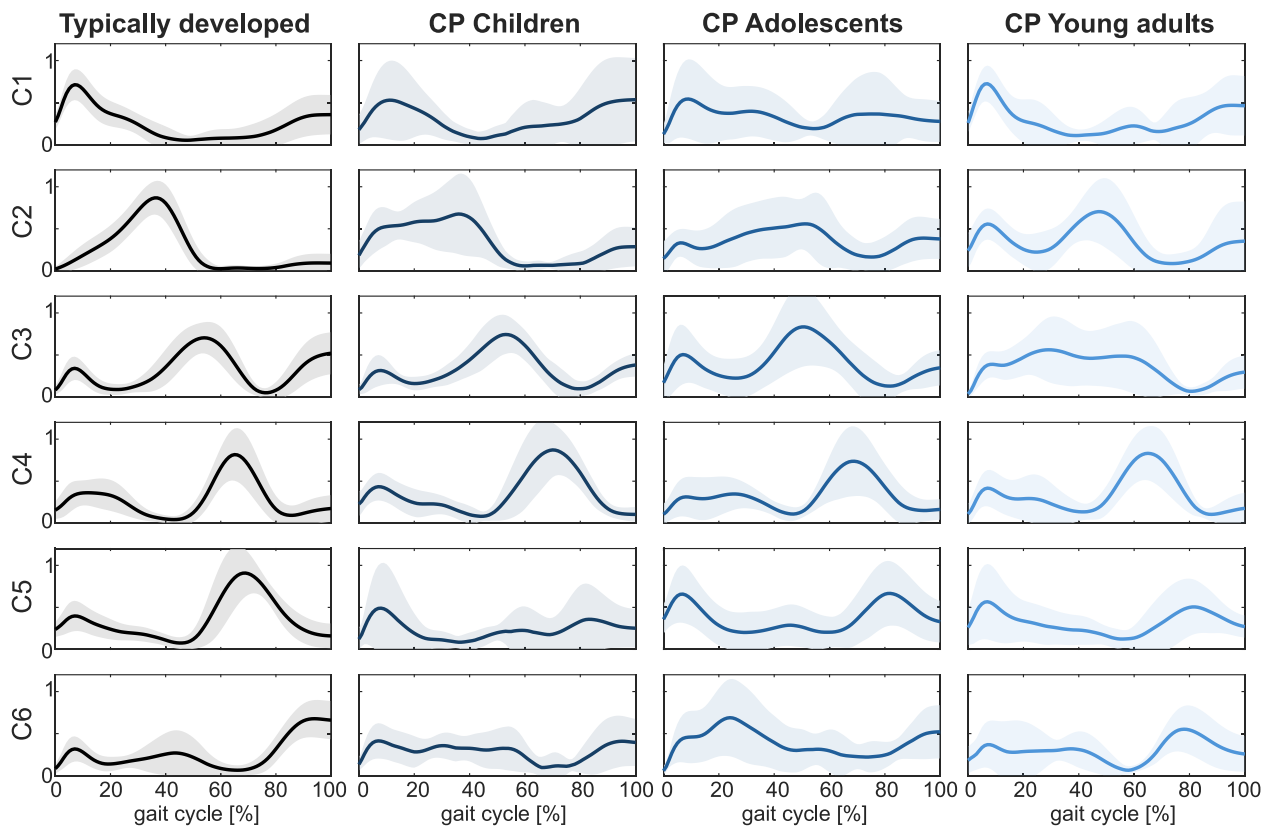


Fig. 4. Temporal coefficients of all groups are reported in columns (TD in black, CP children in dark blue, CP adolescents in blue, and CP young adults in light blue). Bold lines represent the mean temporal coefficient of the cluster, while the shaded areas represent the standard deviation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

closest to TD, while CP adolescents and CP young adults progressively diverged, reflecting disease-related reorganization rather than normal development, as spatiotemporal parameters did not follow typical age-related trends (Voss et al., 2020).

Our findings align with prior studies reporting early stance and late swing deviations in CP, earlier activation of gastrocnemius-dominated synergies, and reduced TA and RF-related activity (Steele et al., 2015). Similar synergy structures were observed by Goudriaan et al. (Goudriaan et al., 2022), although in our analysis, the TA and RF-related synergies appear as distinct modules, reflecting different underlying kinematic functions. Moreover, previous studies suggested that both the number and structure of muscle synergies may serve as markers of the severity of movement disorders (Tang et al., 2019). Finally, broader and flatter temporal activation profiles, previously described in CP, were also observed here, suggesting impaired timing and reduced modulation of muscle recruitment (Cappellini et al., 2020, 2016).

4.3. Age-related evolution of spatial and temporal components of kinematic-muscular synergies

Age-based stratification in CP revealed distinct effects of maturation on spatial and temporal components of kinematic-muscular synergies. Spatial structures were moderately preserved across age groups, despite increased co-activation compared with TD. This suggests that basic modular organization linking muscle activity to biomechanics is established early and remains relatively stable, with differences from TD reflecting long-term adaptations rather than structural reorganization.

In contrast, temporal activation profiles showed clear age-related divergence. Children with CP displayed timing patterns closer to TD, particularly during stance, whereas CP adolescents and CP young adults showed reduced temporal modulation and greater variability, especially in swing-related synergies. This indicates that maturation in CP

primarily affects the timing and scaling of synergy recruitment rather than their composition, consistent with evidence from typical motor development (Dominici et al., 2011; Ivanenko et al., 2013). Temporal differences arise from both changes in waveform structure and phase shifts. For instance, delays in late swing were observed in younger patients, while anticipatory patterns emerged in specific modules in CP young adults. This suggests that maturation in CP is associated not only with increased variability but also with reorganization of the temporal coordination of gait. Moreover, the late swing modules showed the greatest age-related divergence, indicating that more complex and finely tuned phases of gait, such as swing and stride preparation, may be more susceptible to developmental alterations in CP. Changes in synergy timing may also be related to differences in walking speed between patients and TD children. Walking speed could not be experimentally controlled because of the motor limitations of the patients; however, reduced walking velocity is itself a characteristic feature of CP. Therefore, it should not be considered a confounding factor, but rather an intrinsic component of the pathological gait pattern and of the overall motor strategy adopted by these individuals.

Importantly, these age-related differences cannot be explained by typical developmental changes in gait, as spatiotemporal parameters did not follow the maturation trends observed in TD populations (Voss et al., 2020). Instead, progressive temporal alterations likely reflect compensatory strategies, growth-related biomechanical changes, or cumulative deficits in selective motor control, contributing to slower and more cautious gait in older individuals with CP (Johnson et al., 1997). Compensatory strategies include increased co-contraction to enhance joint stability, delayed or prolonged activation to support foot placement, and anticipatory muscle recruitment to facilitate limb advancement and prepare for ground contact. Such adaptations may compensate for impaired selective motor control and contribute to the slower and more cautious gait. Moreover, kinematic-muscular synergies revealed a

Table 3

Intra-cluster similarities of spatial and temporal profiles are reported as mean and standard deviation (in brackets). Means of all the synergies are shown on the right. Inter-cluster similarities of spatial and temporal profiles with respect to the TD group are reported. Inter-cluster cross-correlation is also reported as maximum correlation $r_{\max}$ and Lag% of the patient groups with respect to the TD group (positive = signal is delayed, negative = signal is anticipated).

Spatial synergies: Intra-cluster similarity								
Group		W1	W2	W3	W4	W5	W6	Mean
TD		0.65 (0.21)	0.84 (0.13)	0.66 (0.28)	0.65 (0.23)	0.75 (0.20)	0.54 (0.27)	0.68 (0.10)
CP Children		0.57 (0.21)	0.59 (0.20)	0.72 (0.19)	0.77 (0.17)	0.61 (0.16)	0.43 (0.16)	0.62 (0.12)
CP Adolescents		0.45 (0.27)	0.54 (0.21)	0.65 (0.19)	0.62 (0.16)	0.63 (0.20)	0.56 (0.17)	0.58 (0.07)
CP Young adults		0.58 (0.21)	0.50 (0.25)	0.51 (0.21)	0.64 (0.17)	0.62 (0.17)	0.51 (0.20)	0.56 (0.06)
Temporal coefficients: Intra-cluster correlation								
Group		C1	C2	C3	C4	C5	C6	Mean
TD		0.64 (0.30)	0.85 (0.18)	0.65 (0.25)	0.64 (0.28)	0.65 (0.30)	0.63 (0.27)	0.68 (0.08)
CP Children		0.12 (0.41)	0.45 (0.40)	0.60 (0.30)	0.60 (0.29)	0.03 (0.37)	0.10 (0.31)	0.32 (0.26)
CP Adolescents		0.05 (0.64)	0.10 (0.44)	0.31 (0.47)	0.37 (0.44)	0.27 (0.45)	0.08 (0.57)	0.20 (0.13)
CP Young adults		0.44 (0.29)	0.35 (0.43)	0.21 (0.50)	0.50 (0.51)	0.15 (0.46)	0.21 (0.50)	0.31 (0.14)
Spatial synergies: Inter-cluster similarity								
Group		W1	W2	W3	W4	W5	W6	Mean
CP Children		0.48	0.58	0.66	0.61	0.30	0.41	0.50 (0.14)
CP Adolescents		0.43	0.60	0.50	0.62	0.58	0.38	0.52 (0.10)
CP Young adults		0.52	0.53	0.53	0.54	0.56	0.24	0.49 (0.12)
Temporal coefficients: Inter-cluster correlation								
Group		C1	C2	C3	C4	C5	C6	Mean
CP Children		0.80	0.85	0.93	0.82	0.25	0.57	0.70 (0.25)
CP Adolescents		0.67	0.56	0.84	0.86	0.29	0.21	0.57 (0.27)
CP Young adults		0.92	0.34	0.32	0.96	0.23	0.31	0.51 (0.33)
Temporal coefficients: Inter-cluster circular cross-correlation								
Group		C1	C2	C3	C4	C5	C6	Mean
CP Child.	r _{max}	0.80	0.88	0.93	0.90	0.41	0.57	0.74 (0.21)
	Lag%	0.99	−3.96	0	3.96	38.6	0	6.60 (15.9)
CP Adol.	r _{max}	0.70	0.86	0.84	0.95	0.68	0.62	0.77 (0.13)
	Lag%	1.98	10.9	0	3.96	11.9	32.7	10.2 (12.0)
CP Y. adults	r _{max}	0.92	0.77	0.41	0.96	0.67	0.81	0.76 (0.20)
	Lag%	−0.99	11.9	−30.7	0	11.9	10.9	−3.13(16.0)

dissociation between preserved kinematics and altered muscle recruitment in specific modules. For instance, in W3, the overall kinematic pattern of knee and ankle associated with early swing was maintained, while the underlying muscle activation showed increased co-activation and reduced selectivity. In contrast, other synergies highlighted more evident biomechanical alterations, particularly in CP young adults. In these individuals, knee extension appeared reduced in the whole gait cycle, and hip flexion was temporally shifted, occurring later (i.e., more predominantly in W4 rather than W3). Additionally, increased pelvic anterior tilt was observed toward the end of the gait cycle, suggesting a compensatory contribution to limb advancement. Indeed, studies demonstrated that during maturation, the gait pattern progressively deteriorates in CP individuals, reducing the range of motions, increasing double support (Bell et al., 2002). Overall, spatial structure appears to reflect persistent neuromotor constraints, whereas temporal organization captures age-dependent adaptations. Notably, these temporal changes were not directly associated with GMFCS or FMS levels, since these measures were not different between groups, suggesting that maturation influences how and when motor modules are recruited more than which modules are available.

4.4. Clinical impact of kinematic-muscular synergies

Kinematic-muscular synergies offer a comprehensive framework to

understand gait impairments in children with CP, as they associate neuromuscular activation with the resulting biomechanical execution. While traditional gait analysis often examines muscle activity and movement separately, this integrated model offers insight into the underlying mechanisms of gait deviations. In the context of CP, this approach may provide a more direct interpretation of how altered neural commands generate pathological movement patterns. Specifically, our results showed altered muscle coordination, such as increased co-activation and phase shifts, which in turn lead to inefficient or compensatory kinematic patterns. Unlike muscle synergies, which describe patterns of muscle coordination, kinematic-muscle synergies incorporate both muscle activity and joint-level kinematic contributions. This allows each module to be interpreted not only in terms of neural control but also in terms of its biomechanical function, providing a direct link between altered muscle recruitment and resulting movement patterns. For instance, in W3, we observed preserved kinematic patterns despite altered muscle activation, suggesting compensatory recruitment strategies. Conversely, in W4, altered muscle coordination was associated with measurable changes in joint kinematics, such as reduced knee extension and delayed hip flexion. These distinctions cannot be directly captured using muscle synergies alone. Moreover, identifying abnormal muscle co-activation or altered joint kinematics during a particular gait phase can help clinicians target that specific dysfunction during therapy. For example, in W6, the altered

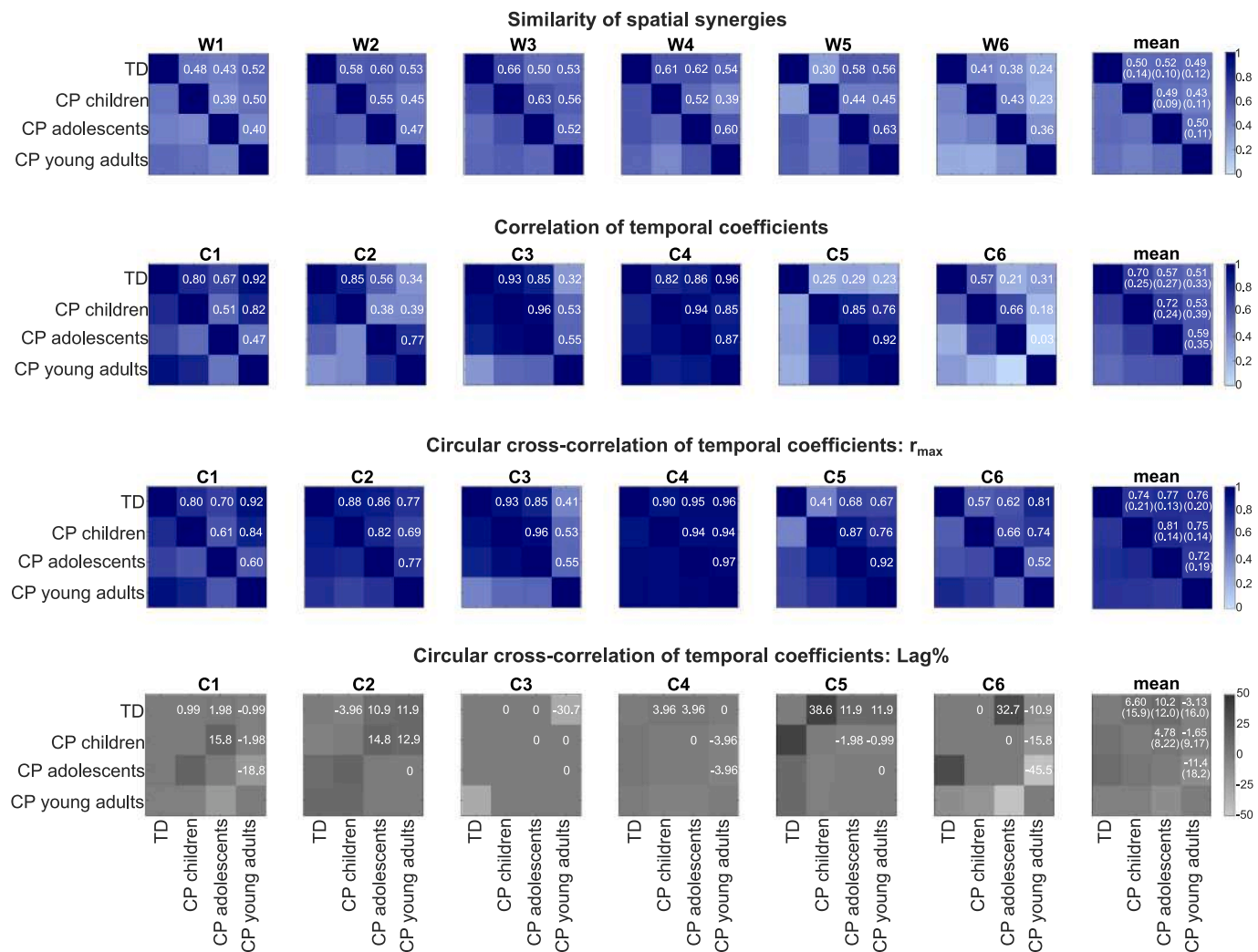


Fig. 5. Color maps show similarity of spatial synergies (first row) and correlation of temporal coefficients (second row) for each synergy across all possible pairs of groups. Means and standard deviations are reported in the last column. In the third row, the maximum value of the cross-correlation $r_{\max}$ is reported, while in the last row, the Lag% is reported. Positive values indicate that the signal is delayed, negative values indicate that the signal is anticipated. The comparisons were CP children with respect to TD group, CP adolescents with respect to TD and CP children, CP young adults with respect to TD, CP children, and adolescents.

organization of muscle activation is associated with increased anterior pelvic tilt and reduced knee flexion during late swing. This provides a functional interpretation of the impairment, linking abnormal muscle recruitment to specific kinematic deviations. From a clinical perspective, this allows clinicians not only to identify when abnormal activation occurs but also to understand how it affects movement. As a result, rehabilitation strategies can be more targeted toward correcting specific biomechanical deficits, such as improving knee control or pelvic stabilization, rather than only reducing co-activation. This functional interpretation may support more informed decisions in physiotherapy planning, orthotic prescription, and specific treatment. Rehabilitation programs can then be designed to improve appropriate muscle recruitment, aiming to restore activation patterns that resemble those of TD children (Kim et al., 2021). Conversely, the preservation of spatial synergy structure in milder gait impairments suggests that these children maintain fundamental neuromotor strategies. Synergy-based metrics may provide practical information for individualized therapeutic goals. Furthermore, integrating synergy analysis into clinical decision-making can enhance the personalization of surgical planning and rehabilitation strategies. For instance, identifying muscles that contribute abnormally to specific synergies can guide selective surgical interventions, such as tendon lengthening or transfers, to rebalance force distribution. Then, specific rehabilitative techniques can be

tailored to reinforce the activation patterns. Additionally, complementary practices such as functional electrical stimulation (FES) may help optimize inter-limb coordination and muscle selectivity based on synergies. Interventions can also be tailored to improve specific kinematic outcomes, such as enhancing knee extension during swing or stabilizing pelvic motion. Finally, the use of orthoses can be fine-tuned according to individual synergy patterns: for example, ankle foot orthoses may assist in modulating inappropriate co-contractions or enhance push-off efficiency in children with weak plantarflexor recruitment.

4.5. Limitations and future work

This study presents some limitations. First, although the use of 16 EMG channels (8 per limb) aligns with the standard practice in the literature (Safavynia and Ting, 2012), the coverage remains limited relative to the total number of muscles involved in lower-limb motor control. Prior studies have emphasized that restricting the number of recorded muscles may lead to missing or misinterpreting certain synergies (Brambilla and Scano, 2022; Steele et al., 2013). Increasing the number of muscles would improve synergy representation. Second, only four sagittal plane joint kinematic profiles were included in the modular decomposition. Future work should consider additional degrees of freedom, particularly in the medio-lateral plane, to have a more

comprehensive characterization of gait deviations. Furthermore, the limited number of gait cycles used for the analysis may have influenced the robustness of synergy extraction. Future studies should investigate the impact of the number of gait cycles on synergy-related outcomes. Moreover, in clinical and pediatric populations, maximizing the number of cycles may introduce artifacts due to fatigue or reduced compliance, which can significantly bias the synergy results. Third, the sample size, particularly within each CP subgroup, was relatively small, affecting the robustness of the comparisons. Moreover, sex distribution was not balanced in TD participants and patients. Although sex-related differences in gait were not the primary focus of this study, they may affect the generalizability of the findings. Larger and more balanced cohorts would improve statistical power and strengthen the generalizability of the findings. Moreover, CP subtypes were not evenly distributed across age groups, with more hemiparetic patients in the younger cohort. Hemiparesis is often associated with higher functional mobility compared to diplegia, which may have partially biased the synergy parameters in the CP children group. However, age-based stratification was prioritized to capture the developmental trajectory of motor control. Future research with larger, subtype-balanced cohorts is needed to disentangle the relative contributions of clinical diagnosis and neuro-motor maturation.

5. Conclusions

This work demonstrates that kinematic-muscular synergies can provide insights into motor control in children with CP. Indeed, spatial synergy structures were partially preserved across gait patterns, exhibiting higher muscle co-contractions. However, patients showed changes in the temporal activation with age, suggesting reduced coordination in the timing of biomechanical functions. These results highlight the value of kinematic-muscular synergies as a tool to evaluate functional gait impairments.

CRediT authorship contribution statement

Cristina Brambilla: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Alessandro Scano:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Giulia Beltrame:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Giorgia Marino:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Luigi Piccinini:** Writing – review & editing, Supervision, Project administration, Investigation. **Lorenzo Molinari Tosatti:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition. **Nicola Portinaro:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Humanitas Research Hospital, Milan, Italy (protocol code 3204 and date of approval 02/02/2022).

Informed consent was obtained from all participants involved in the study. Written informed consent has been obtained from the patients to publish this paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The datasets used and analyzed in the current study are available from the corresponding author on reasonable request and pending Ethical Approval.

References

- Barroso, F.O., Torricelli, D., Bravo-Esteban, E., Taylor, J., Gómez-Soriano, J., Santos, C., et al., 2016. Muscle synergies in cycling after incomplete spinal cord injury: correlation with clinical measures of motor function and spasticity. *Front. Hum. Neurosci.* 9. <https://doi.org/10.3389/fnhum.2015.00706>.
- Bekius, A., Bach, M.M., van der Krogt, M.M., de Vries, R., Buizer, A.I., Dominici, N., 2020. Muscle synergies during walking in children with cerebral palsy: a systematic review. *Front. Physiol.* 11, 632. <https://doi.org/10.3389/fphys.2020.00632>.
- Bell, K.J., Öunpuu, S., DeLuca, P.A., Romness, M.J., 2002. Natural progression of gait in children with cerebral palsy. *J. Pediatr. Orthop.* 22, 677.
- Beltrame, G., Scano, A., Marino, G., Peccati, A., Molinari Tosatti, L., Portinaro, N., 2023. Recent developments in muscle synergy analysis in young people with neurodevelopmental diseases: a systematic review. *Front. Bioeng. Biotechnol.* 11.
- Bizzi, E., Cheung, V.C.K., d'Avella, A., Saltiel, P., Tresch, M., 2008. Combining modules for movement. *Brain Res. Rev.* 57, 125–133. <https://doi.org/10.1016/j.brainresrev.2007.08.004>.
- Bowden, M.G., Clark, D.J., Kautz, S.A., 2010. Evaluation of abnormal synergy patterns poststroke: relationship of the Fugl-Meyer assessment to hemiparetic locomotion. *Neurorehabil. Neural Repair* 24, 328–337. <https://doi.org/10.1177/1545968309343215>.
- Brambilla, C., Scano, A., 2022. The number and structure of muscle synergies depend on the number of recorded muscles: a pilot simulation study with OpenSim. *Sensors (Basel)* 22, 8584. <https://doi.org/10.3390/s22228584>.
- Cappellini, G., Ivanenko, Y.P., Poppele, R.E., Lacquaniti, F., 2006. Motor patterns in human walking and running. *J. Neurophysiol.* 95, 3426–3437. <https://doi.org/10.1152/jn.00081.2006>.
- Cappellini, G., Ivanenko, Y.P., Martino, G., MacLellan, M.J., Sacco, A., Morelli, D., et al., 2016. Immature spinal locomotor output in children with cerebral palsy. *Front. Physiol.* 7. <https://doi.org/10.3389/fphys.2016.00478>.
- Cappellini, G., Sylos-Labini, F., Dewolf, A.H., Solopova, I.A., Morelli, D., Lacquaniti, F., et al., 2020. Maturation of the locomotor circuitry in children with cerebral palsy. *Front. Bioeng. Biotechnol.* 8. <https://doi.org/10.3389/fbioe.2020.00998>.
- Chia Bejarano, N., Pedrocchi, A., Nardone, A., Schieppati, M., Baccinelli, W., Monticone, M., et al., 2017. Tuning of muscle synergies during walking along rectilinear and curvilinear trajectories in humans. *Ann. Biomed. Eng.* 45, 1204–1218. <https://doi.org/10.1007/s10439-017-1802-z>.
- Chvatal, S.A., Ting, L.H., 2013. Common muscle synergies for balance and walking. *Front. Comput. Neurosci.* 7, 48. <https://doi.org/10.3389/fncom.2013.00048>.
- d'Avella, A., Portone, A., Fernandez, L., Lacquaniti, F., 2006. Control of fast-reaching movements by muscle synergy combinations. *J. Neurosci.* 26, 7791–7810. <https://doi.org/10.1523/JNEUROSCI.0830-06.2006>.
- Dominici, N., Ivanenko, Y.P., Cappellini, G., d'Avella, A., Mondì, V., Cicchese, M., et al., 2011. Locomotor primitives in newborn babies and their development. *Science* 334, 997–999. <https://doi.org/10.1126/science.1210617>.
- Fellin, R.E., Rose, W.C., Royer, T.D., Davis, I.S., 2010. Comparison of methods for kinematic identification of footstrike and toe-off during overground and treadmill running. *J. Sci. Med. Sport* 13, 646–650. <https://doi.org/10.1016/j.jsams.2010.03.006>.
- Frère, J., Hug, F., 2012. Between-subject variability of muscle synergies during a complex motor skill. *Front. Comput. Neurosci.* 6. <https://doi.org/10.3389/fncom.2012.00099>.
- Ghislieri, M., Agostini, V., Knaflitz, M., 2020. Muscle synergies extracted using principal activations: improvement of robustness and interpretability. *IEEE Trans. Neural Syst. Rehabil. Eng.* 28, 453–460. <https://doi.org/10.1109/TNSRE.2020.2965179>.
- Goudriaan, M., Papageorgiou, E., Shuman, B.R., Steele, K.M., Dominici, N., Van Campenhout, A., et al., 2022. Muscle synergy structure and gait patterns in children with spastic cerebral palsy. *Dev. Med. Child Neurol.* 64, 462–468. <https://doi.org/10.1111/dmcn.15068>.
- Graham, H.K., Harvey, A., Rodda, J., Nattrass, G.R., Pipiris, M., 2004. The functional mobility scale (FMS). *J. Pediatr. Orthop.* 24, 514.
- Hermens, H.J., Freriks, B., Disselhorst-Klug, C., Rau, G., 2000. Development of recommendations for SEMG sensors and sensor placement procedures.

- J. Electromyogr. Kinesiol. 10, 361–374. [https://doi.org/10.1016/S1050-6411\(00\)00027-4](https://doi.org/10.1016/S1050-6411(00)00027-4).
- Ivanenko, Y.P., Poppele, R.E., Lacquaniti, F., 2004. Five basic muscle activation patterns account for muscle activity during human locomotion. *J. Physiol.* 556, 267–282. <https://doi.org/10.1113/jphysiol.2003.057174>.
- Ivanenko, Y.P., Dominici, N., Cappellini, G., Paolo, A.D., Giannini, C., Poppele, R.E., et al., 2013. Changes in the spinal segmental motor output for stepping during development from infant to adult. *J. Neurosci.* 33, 3025–3036. <https://doi.org/10.1523/JNEUROSCI.2722-12.2013>.
- Johnson, D.C., Damiano, D.L., Abel, M.F., 1997. The evolution of gait in childhood and adolescent cerebral palsy. *J. Pediatr. Orthop.* 17, 392.
- Kaufmann, P., Koller, W., Wallnöfer, E., Gonçalves, B., Baca, A., Kainz, H., 2024. Increased trial-to-trial similarity and reduced temporal overlap of muscle synergy activation coefficients manifest during learning and with increasing movement proficiency. *Sci. Rep.* 14, 17638. <https://doi.org/10.1038/s41598-024-68515-3>.
- Kim, Y., Bulea, T.C., Damiano, D.L., 2018. Children with cerebral palsy have greater stride-to-stride variability of muscle synergies during gait than typically developing children: implications for motor control complexity. *Neurorehabil. Neural Repair* 32, 834–844. <https://doi.org/10.1177/1545968318796333>.
- Kim, Y., Bulea, T.C., Damiano, D.L., 2021. Greater reliance on cerebral palsy-specific muscle synergies during gait relates to poorer temporal-spatial performance measures. *Front. Physiol.* 12, 630627. <https://doi.org/10.3389/fphys.2021.630627>.
- Lanzani, V., Brambilla, C., Scano, A., 2024. Kinematic-muscular synergies describe human locomotion with a set of functional synergies. *Biomimetics* 9, 619. <https://doi.org/10.3390/biomimetics9100619>.
- Lee, D.D., Seung, H.S., 1999. Learning the parts of objects by non-negative matrix factorization. *Nature* 401, 788–791. <https://doi.org/10.1038/44565>.
- Marino, G., Scano, A., Beltrame, G., Brambilla, C., Marazzi, A., Aparo, F., et al., 2024. Influence of backpack carriage and walking speed on muscle synergies in healthy children. *Bioengineering* 11, 173. <https://doi.org/10.3390/bioengineering11020173>.
- Palisano, R., Rosenbaum, P., Walter, S., Russell, D., Wood, E., Galuppi, B., 1997. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev. Med. Child Neurol.* 39, 214–223. <https://doi.org/10.1111/j.1469-8749.1997.tb07414.x>.
- Patel, D.R., Bovid, K.M., Rausch, R., Ergun-Longmire, B., Goetting, M., Merrick, J., 2024. Cerebral palsy in children: a clinical practice review. *Curr. Probl. Pediatr. Adolesc. Health Care* 54, 101673. <https://doi.org/10.1016/j.cppeds.2024.101673>.
- Rimini, D., Agostini, V., Knaflitz, M., 2017. Intra-subject consistency during locomotion: similarity in shared and subject-specific muscle synergies. *Front. Hum. Neurosci.* 11, 586. <https://doi.org/10.3389/fnhum.2017.00586>.
- Rosenbaum, P., Paneth, N., Leviton, A., Goldstein, M., Bax, M., Damiano, D., et al., 2007. A report: the definition and classification of cerebral palsy April 2006. *Dev. Med. Child Neurol. Suppl.* 109, 8–14.
- Russo, M., Scano, A., Brambilla, C., d'Avella, A., 2024. SynergyAnalyzer: a Matlab toolbox implementing mixed-matrix factorization to identify kinematic-muscular synergies. *Comput. Methods Prog. Biomed.* 251, 108217. <https://doi.org/10.1016/j.cmpb.2024.108217>.
- Safavynia, S.A., Ting, L.H., 2012. Task-level feedback can explain temporal recruitment of spatially fixed muscle synergies throughout postural perturbations. *J. Neurophysiol.* 107, 159–177. <https://doi.org/10.1152/jn.00653.2011>.
- Scano, A., Mira, R.M., d'Avella, A., 2022. Mixed matrix factorization: a novel algorithm for the extraction of kinematic-muscular synergies. *J. Neurophysiol.* 127, 529–547. <https://doi.org/10.1152/jn.00379.2021>.
- Shuman, B., Goudriaan, M., Bar-On, L., Schwartz, M.H., Desloovere, K., Steele, K.M., 2016. Repeatability of muscle synergies within and between days for typically developing children and children with cerebral palsy. *Gait Posture* 45, 127–132. <https://doi.org/10.1016/j.gaitpost.2016.01.011>.
- Steele, K.M., Tresch, M.C., Perreault, E.J., 2013. The number and choice of muscles impact the results of muscle synergy analyses. *Front. Comput. Neurosci.* 7. <https://doi.org/10.3389/fncom.2013.00105>.
- Steele, K.M., Rozumalski, A., Schwartz, M.H., 2015. Muscle synergies and complexity of neuromuscular control during gait in cerebral palsy. *Dev. Med. Child Neurol.* 57, 1176–1182. <https://doi.org/10.1111/dmcn.12826>.
- Steele, K.M., Munger, M.E., Peters, K.M., Shuman, B.R., Schwartz, M.H., 2019. Repeatability of electromyography recordings and muscle synergies during gait among children with cerebral palsy. *Gait Posture* 67, 290–295. <https://doi.org/10.1016/j.gaitpost.2018.10.009>.
- Tang, S., Chen, L., Barsotti, M., Hu, L., Li, Y., Wu, X., et al., 2019. Kinematic synergy of multi-DoF movement in upper limb and its application for rehabilitation exoskeleton motion planning. *Front. Neurobot.* 13, 99. <https://doi.org/10.3389/fnbot.2019.00099>.
- Voss, S., Joyce, J., Biskis, A., Parulekar, M., Armijo, N., Zampieri, C., et al., 2020. Normative database of spatiotemporal gait parameters using inertial sensors in typically developing children and young adults. *Gait Posture* 80, 206–213. <https://doi.org/10.1016/j.gaitpost.2020.05.010>.
- Wood, E., Rosenbaum, P., 2000. The gross motor function classification system for cerebral palsy: a study of reliability and stability over time. *Dev. Med. Child Neurol.* 42, 292–296. <https://doi.org/10.1017/s0012162200000529>.
- Xiong, Q., Wan, J., Jiang, S., Liu, Y., 2022. Age-related differences in gait symmetry obtained from kinematic synergies and muscle synergies of lower limbs during childhood. *Biomed. Eng. Online* 21, 61. <https://doi.org/10.1186/s12938-022-01034-2>.