Pregnancy-related changes in center of pressure during gait

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Purpose: Physical and hormonal modifications occurring during the pregnancy, can lead to an increase in postural instability and to a higher risk of falls during gait. The first objective was to describe the center of pressure (COP) during late pregnancy at different gait velocity. Comparison of nulliparous women with postpartum women were conducted in order to investigate the effects of pregnancy on gait variability. Methods: Fifty-eight pregnant women in the last four months of pregnancy, nine postpartum women and twenty-three healthy non-pregnant women performed gait trials at three different speeds: preferred, slow and fast. Results: In the last four months of pregnancy gait velocity decreased. During the pregnancy, gait velocity decreased by 22%, stopover time increased by 6–12%, COP excursion XY decreased by 5% and COP velocity decreased by 16% and 20% along the anteroposterior and transverse axes, respectively. After delivery, gait velocity increased by 3% but remained a lower compared to non-pregnant women (–12%). Intra-individual variability was greater for non-pregnant than pregnant women. Conclusions: COP parameters were influenced by pregnancy. This suggests that pregnant women establish very specific and individual strategies with the aim of maintaining stability during gait.

Key words: pregnancy, gait, centre of pressure

1. Introduction

During the pregnancy, physical and hormonal modifications occur, including weight gain [1], increased ligament laxity [20], alterations in skeletal alignment, disturbed neuromuscular control and muscle strength [16]. These changes can lead to an increase in postural instability causing a significant change in oscillations, imposing on pregnant woman to use specific strategies to maintain adequate posture [9], [29]. A decrease in stability leads to a higher risk of falls during gait and the percentage of falls during pregnancy is relatively high, reaching 27% [12]. The risks are significantly higher in the third trimester compared to the first and second trimester [22].

To evaluate gait, spatial and temporal parameters were analyzed in several studies. Few studies have assessed the center of pressure (COP) during gait,

although it seems reliable for assessing gait and balance (ICC: 0.80) [29], [30].

For spatial and temporal gait parameters during pregnancy, according to several authors [2], [15], gait remains unchanged with similar speed, cadence, stride length and stable kinematic parameters. For Forczek et al. [14] and Gottschall et al. [18], the gait of pregnant women undergoes modification. A slower gait, with a decrease in walking frequency and stride length and increased step variability were observed [13], [14], [18]. There is an increase in double support time compared to post-partum and nulliparous women. These are fine adjustments that minimize the time on one leg to reduce muscle solicitation [7], [15]. Thus, pregnant women exaggerate transition phases in order to increase the security of gait, similarly to what was shown previously for level and inclined surface gait [18]. The lack of consensus may be related to a large variability in gait strategies and different adaptations to pregnancy [14], [15].

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96 J. Bertuit et al.

In order to study COP during gait Lymbery and Gilleard [25] evaluated thirteen pregnant women at 38 weeks of gestation and 8 weeks postpartum. The length of COP was changed in late pregnancy explained by an increase of step width. Medio-lateral COP displacements tended to be larger, compared to post-partum, potentially because of a difficulty of pregnant women to control balance due to increased mass. This study results suggest that pregnant women adapt different gait parameter in order to maximize stance phase stability and to control medio-lateral displacement [25], [28]. However, McCrory et al. [27] did not observe any difference in medio-lateral COP displacement between trimesters and groups of pregnant or nonpregnant women. Once again, a lack of consensus was observed, thus limiting the understanding of pregnant gait.

In relation to the various results and the paucity of study in the field, it seems necessary to investigate the issue of pregnant women gait for a better therapeutic understanding and follow-up. In fact, knowing healthy pregnant women motor strategies is fundamental for the management and follow-up of pregnant women with pain during gait.

The first objective of the study was to describe COP during late pregnancy. Comparisons with nulliparous women and post-partum women were conducted in order to investigate the effects of pregnancy on COP parameters during gait. The second objective was to analyse COP variability between pregnant and non-pregnant women in order to investigate the effects of pregnancy on gait variability.

2. Materials and methods

Participants

The characteristics of the sample being tested are presented in Table 1. Fifty-eight pregnant women (preg-

nant group – PG) aged between 25 and 41 years, with no history of foot, ankle or knee musculoskeletal pain, no pelvic girdle pain, no neuromuscular trauma or disease and no cardiovascular problems participated in this study. Twin pregnancies and pregnancies with complications were also exclusion criteria. The subjects were divided into 4 groups: (1) 6th month (25 to 28 amenorrhea gestation weeks), (2) 7th month (29 to 32 amenorrhea gestational weeks), (3) 8th month (33 to 36 amenorrhea gestational weeks) and (4) 9th month (37 to 41 amenorrhea gestational weeks). Among pregnant women 59% worked, 28% did not work and 13% were students. 71% of all women being tested had no children, 27% had one child and 2% had two or more children.

The postpartum women group (postpartum group – PPG) was formed by 9 subjects (4 to 8 months after delivery). The pregnant and postpartum participants were recruited via direct contact during preand post-natal gym classes organised in the University hospital.

Twenty-three healthy nulligravidae women (control group – CG) aged between 21 and 38 years agreed to take part in the study as control group (CG). No differences in age and height were found between groups. All subjects gave written informed consent prior to participation in the study approved by the local Ethics Committee. The recruitment of subjects took place between January 2009 and December 2011.

Material

COP parameters during gait were measured using the GAITRite electronic walkway (GAITRite Gold, CIR Systems, PA, USA, length: 6.1 m, width: 61 cm), with embedded pressure sensors formed in horizontal grid. Data was sampled at a frequency of 100 Hz. The walkway was connected to a PC by a serial interface cable. COP characteristics were processed and stored using GAITRite GOLD, version 3.2b software and processed by Excel 2007 software.

Table 1. Characteristics of pregnant group (PG), post-partum group (PPG) and control group (CG). Mean (SD)

	Months	Number of subject	Age [years]	Height [cm]	Mass [Kg]	BMI [kg/m ²]	BMI [kg/m ²]	Mass gain
						before pregnancy	during test	[kg]
	6	8	26 (1)	168 (6)	72 (9)	23 (3)	25 (3)	8 (4)
	7	17	28 (5)	165 (6)	70 (9)	22 (3)	26 (3)	11 (3)
PG	8	23	30 (6)	165 (6)	73 (10)	23 (6)	28 (6)	10 (4)
	9	10	29 (3)	168 (7)	73 (8)	19 (7)	26 (3)	12 (4)
		58	29 (5)	166 (6)	62 (11)	22 (5)	27 (5)	10 (4)
PPG		9	31 (6)	167 (6)	74 (19)		26 (6)	
GC		23	27 (5)	168 (6)	63 (10)		22 (3)	

Methods

Before performing the motor task, anthropometric data (age, shoe size, body mass and height) were recorded for each subject. The length of the lower limbs (from the anterior-superior iliac spine to the medial malleolus) was determined with a tape when lying down.

The motor task consisted of 9 gait trials (3 at each speed: fast, preferred and slow) on the GAITRite walkway. To counter the methodological bias of acceleration and deceleration in gait, participants started walking 2 m ahead of the walkway and finished the trial 2 m after the end of the walkway.

A rest period was allowed between trials. First, the subject was invited to walk at her preferred speed. Then, the subjects walked at fast and slow speed. The order of the trials was randomised by dice throwing. The instructions for fast speed were "walk as fast as possible. As if you would catch a bus" and the instructions for slow speed were "walk slowly. As if you were shopping".

Data processing

Relative coordinates (x, y) of COP trajectory were calculated from the absolute coordinates (x, y).

The following parameters were calculated: stance time, COP excursion, COP velocity, COP length and COP width. Stance time (ST) was defined as ST = $T_{\text{max}} - T_{\text{min}}$, where T_{min} and T_{max} corresponded to the first and last instants of stance phase. COP excursion was defined as the absolute displacements between two successive COP in anteroposterior (AP–X axis) or medio-lateral (ML-Y axis) direction. Also, the distance between two successive positions of COP in the plane formed by X and Y axes (AP-ML) was computed and expressed in metres. COP velocity X corresponded to the velocity of COP displacement in anteroposterior (AP–X axis), medio-lateral (ML–Y axis) direction or the XY plane (AP–ML) and is defined as V = X or Y or $XY / (T_{n+1} - T_n)$ where T is the time between two successive positions of the COP. It was expressed in metres per second. COP Length X (AP) (LX) was defined by $LX = x_{max} - x_{min}$, where x_{max} and x_{\min} represent the largest and smallest x coordinates of the COP. COP width Y (ML) (LY) was defined by $LY = y_{\text{max}} - y_{\text{min}}$, where y_{max} and y_{min} represent the largest and smallest y coordinates of the COP.

After that the variables calculated before were analysed statistically.

Statistical Analysis

All statistical procedures were conducted using Statistica 5.0 software for Windows. To investigate

normal distribution of data the Kolmogorov-Smirnov test was used. All scores were found to be normally distributed. A Student's t-test for paired samples did not show a significant difference between sides: data of left and right feet were thus averaged. For the effect of pregnancy, an analysis of variance for repeated measures (ANOVA) was performed in order to compare all variables between the different speeds (within group factor) and groups (between groups factor). When a significant effect was found, the LSD post hoc test was applied (between months of pregnancy or PG/GC, PG/PPG, and PPG/CG). The statistical level of significance was set at 0.05. To investigate relationships between parameters the Pearson coefficient of correlation of "r" was used. The coefficient of variation (in %) was used to analyse the variability and an analysis of variance for repeated was used to compare of all variables between the different speeds and groups (between PG and CG)

3. Results

Comparison between the last four months of pregnancy

The results of velocity parameters for the last 4 months of pregnancy are shown in Table 2. During the pregnancy, a significant evolution of velocity (p = 0.032) was observed. Velocity decreased between the 6th and 7th months of pregnancy at slow speed (p = 0.034) and increased between the 8th and 9th months at fast speed (p = 0.013).

The results of COP parameters are shown in Table 3 coupled with month's effect. None of the parameters of COP changed significantly between the last 4 months of pregnancy.

Comparison between groups
$$(PG - PPG - CG)$$

The results of velocity parameters for the 3 groups are shown in Table 2.

Velocity: At each speed, PG walked more slowly than GC: by 20% at preferred speed (p < 0.001), by 22% at fast speed (p < 0.001) and by 12% at slow speed (p = 0.017). No significant difference between PG and PPG was found at preferred and slow speed. At fast speed, however, PG displayed reduced velocity by 15% compared to PPG (p < 0.001). After child-birth, a lower preferred gait velocity was seen (by 12%, p = 0.021). COP parameters results of different groups are shown in Table 3. A group effect was ob-

J. Bertuit et al.

Table 2. Mean (SD) gait velocity (m/s) during pregnancy (PG), in post-partum (PPG) and for control group (CG)

Speed	PG – months				P value				P value			
	6	7	8	9	groups effect	PG	PPG	CG	Groups effect	PG Vs CG	PG Vs PPG	PPG Vs CG
S	0.8 (0.12)	0.65 (0.28)	0.7 (0.20)	0.79 (0.14)	0.032	0.71 (0.21)	0.8 (0.27)	0.81 (0.13)	<0.001	0.017	0.138	0.881
P	1.05 (0.12)	0.92 (0.17)	1.00 (0.13)	1.04 (0.2)		0.99 (0.16)	1.11 (0.14)	1.26 (0.13)		< 0.001	0.051	0.021
F	1.40 (0.08)	1.32 (0.31)	1.39 (0.18)	1.56 (0.23)		1.4 (0.24)	1.64 (0.21)	1.76 (0.22)		< 0.001	<0.001	0.082

Speed: S - slow, P - preferred, F - fast.

Table 3. Mean (SD) COP parameters during pregnancy (PG), post-partum (PPG) and for control group (CG)

			p value							
	Speed	PG	PPG	CG	Velocity	Months	Groups	PG Vs CG	PG Vs PPG	PPG Vs CG
G:	S	0.90 (0.15)	0.81 (0.11)	0.84 (0.12)		0.64	0.001	0.001	0.096	0.527
Stance time [s]	P	0.72 (0.10)	0.69 (0.06)	0.63 (0.06)	< 0.001					
[9]	F	0.58 (0.07)	0.54 (0.05)	0.51 (0.05)						
A.D	S	0.18 (0.01)	0.18 (0.01)	0.18 (0.02)						
AP excursion [m]	P	0.18 (0.01)	0.18 (0.01)	0.18 (0.01)	0.20	0.97	0.07			
[III]	F	0.18 (0.01)	0.18 (0.01)	0.018 (0.001)						
MLE .	S	0.07 (0.01)	0.07 (0.01)	0.07 (0.01)		0.08	0.07			
ML Excursion [m]	P	0.06 (0.01)	0.06 (0.01)	0.06 (0.01)	< 0.001					
[III]	F	0.05 (0.01)	0.06 (0.01)	0.06 (0.01)						
AP-ML	S	0.20 (0.02)	0.21 (0.01)	0.21 (0.02)	0.003	0.76	0.009			
excursion	P	0.19 (0.01)	0.20 (0.01)	0.20 (0.01)				0.003	0.126	0.701
[m]	F	0.19 (0.01)	0.20 (0.01)	0.20 (0.02)						
AD 1 %	S	0.21 (0.03)	0.23 (0.04)	0.23 (0.03)	<0.001	0.35	<0.001	< 0.001	0.022	0.186
AP velocity [m/s]	P	0.25 (0.03)	0.26 (0.03)	0.30 (0.03)						
[111/8]	F	0.31 (0.04)	0.34 (0.04)	0.36 (0.04)						
MI 1 '	S	0.08 (0.01)	0.09 (0.01)	0.09 (0.01)		0.28	<0.001	< 0.001	0.161	0.073
ML velocity [m/s]	P	0.08 (0.01)	0.09 (0.01)	0.10 (0.02)	< 0.001					
[111/8]	F	0.10 (0.02)	0.11 (0.02)	0.12 (0.03)						
AP-ML	S	0.23 (0.03)	0.26 (0.04)	0.26 (0.03)		0.40	<0.001			
velocity	P	0.28 (0.03)	0.29 (0.03)	0.33 (0.04)	< 0.001			< 0.001	0.022	0.092
[m/s]	F	0.34 (0.05)	0.38 (0.04)	0.40 (0.05)						
1 d cop	S	0.16 (0.01)	0.17 (0.01)	0.16 (0.01)		0.91	0.15			
Length COP [m]	P	0.16 (0.01)	0.17 (0.01)	0.16 (0.01)	< 0.001					
[111]	F	0.19 (0.01)	0.18 (0.01)	0.17 (0.01)						
W' 1d COP	S	0.03 (0.01)	0.03 (0.00)	0.03 (0.00)		0.44	0.48			
Width COP [m]	P	0.03 (0.01)	0.03 (0.00)	0.03 (0.00)	< 0.001					
Liiij	F	0.02 (0.01)	0.03 (0.00)	0.03 (0.01)	·					

Speed: S = slow, P = preferred, F = fast. AP: anteroposterior, ML: medio-lateral.

served for five parameters: stance time, AP-ML excursion, AP velocity, ML velocity and AP-ML velocity.

In the case of stance time PG differed significantly from CG (p < 0.001) for the three speeds. In PG,

stance time increased from 0,06 to 0,09 sec depending on speed, which represented an increase of 6% at slow speed and 12% for preferred and fast speeds. There were no significant differences when comparing the other groups.

In the case of AP-ML excursion PG differed significantly from CG (p=0.003) for the three speeds with a reduced COP displacement in PPG by 0.01 m (or 5%) for each speed. There were no significant differences for comparing the other groups.

As for as AP velocity was concerned, PG differed significantly from CG (p < 0.001). The velocity of COP displacement on the AP axis was decreased by 8% at slow speed, by 16% at preferred speed and by 14% at fast speed. PG also differed significantly from PPG (p = 0.022). The velocity was decreased in the case of PG compared to PPG by 8% for slow and fast speeds and by 3% for the preferred speed. There were no significant differences in the case of other comparisons.

In the case of ML velocity, PG differed significantly from the CG (p < 0.001). COP velocity along the ML axis decreased in PG by 11, 20 and 16% at low, preferred and fast speed, respectively. There was no significant difference for other comparisons.

As far as the AP-ML velocity was concerned, a significant decrease of AP-ML velocity was found in PG, compared to CG (p < 0.001). PG displayed decreased velocity compared to PPG (p = 0.023), but no significant difference was found between PPG and GC.

The other parameters did not change significantly between groups being compared.

The correlation between COP parameters and gait speed was evaluated using Pearson r coefficient. A significant correlation of gait speed with stance time (r = -0.75) and COP velocity (r = 0.77) was observed.

Study of variability

The results of COP variability are shown in Table 4. There was a significant difference in intra-individual variability between PG and the CG, except for the stance time for which intra-individual variability was greater for the CG than PG.

4. Discussion

COP comparison between the last four months of pregnancy

The decrease in speed between the 6th and the 7th month during slow walking was by 19%. The results are in accordance with the literature [4], [14]. The first explanation is mass. PG had a weight gain of 11 ± 3 kg in the seventh month, which corresponds to the largest mass gain. The increase in abdominal mass of pregnant women modifies posture, which may results in instability during gait. Secondly, Holt et al. [21] showed that the choice of the gait speed is made to provide maximum stability and energetic optimum. Additionally, several authors [11] have shown that slower walking speed is correlated with greater stability. Thus, pregnant women might decrease the optimal speed gait but do not spontaneously choose a gait pattern at lower energy cost, preferring to choose a safe gait associated with greater stability.

For COP parameter, there was no significant difference in the last four months of pregnancy. These results corroborate those of McCrory et al. [26], who showed no change in COP displacement and ground reaction forces (GRF) during advancing pregnancy. All of these data lead us to believe that the COP is stable during the last trimester of pregnancy. We can hypothesize that gait adaptations were realised before the 3rd trimester.

COP comparison between pregnant and non pregnant women

Pregnant women walked more slowly (0.99 \pm 0.16 m/sec at preferred speed) compared to nulliparous women (1.26 \pm 0.13 m/sec). There was a decrease of 22% at preferred speed and of 20% at fast

Table 4. Comparison of COP variability in pregnancy (PG) and for control group (CG) (in terms of coefficient of variation in %)

	Speed	Stance time	AP excursion	ML excursion	AP-ML excursion	AP velocity	ML velocity	AP-ML velocity	Length COP	Width COP
PG	S	5	5	9	5	7	9	7	4	15
	P	5	4	10	4	5	10	5	4	16
	F	5	4	11	4	5	11	5	4	16
	S	8	6	13	6	8	13	8	5	19
CG	P	8	6	12	6	7	12	7	5	17
	F	7	5	14	6	6	14	6	5	19
P value	Groups	0.062	<.001	< 0.001	< 0.001	0.012	< 0.001	0.003	0.017	0.017
r value	Velocity	0.020	0.31	0.042	0.08	0.013	< 0.001	0.010	0.87	0.38

Speed: S - slow, P - preferred, F - fast. AP: anteroposterior, ML: medio-lateral.

J. Bertuit et al.

speed. The results are similar to those found in the study of Lymbery and Gilleard [25] with values of 1.18 ± 0.2 m/s. In the present study, women had an average mass gain of 10.3 kg or 14% during their pregnancy. The decrease in speed may be correlated with the increase in body mass, as the maximum mass increase occurs during the last trimester. However, in our study we found no correlation between gait speed and mass gain during pregnancy, although weight accuracy cannot be guaranteed as women only verbally indicated their weight during the experimental session. This led us to our previous hypothesis: the dominant strategy adopted by pregnant women maximizes safety and stability with greater energy cost during gait [14] due to the fact that stability may be compromised at fast speed. With increasing gait velocity, stance time decreased (r = -0.75) and COP velocity increased (r = 0.77). Furthermore, COP velocity along AP and ML axes was significantly slower, especially at preferred speed where a decrease by 16 to 20% was observed. For Nyska et al. [28], a longer stance time indicates some difficulty in balance during gait. The changes observed hereby are consistent with this statement and probably aimed at increasing the stability of pregnant women with a lower velocity.

For AP COP displacement, no significant group effects were observed. One explanation can be found in the direct link with foot length, unchanged during pregnancy. Several authors [3], [5], evaluating the footprints of pregnant women, found that length, width and angle of the foot did not change during pregnancy. Nevertheless, one must remain cautious with the study of Bird et al. [5], where the evaluation of women was realized during the 12th week of gestation and 4 weeks after childbirth, what does not give an overview of the evolution during gestation. For ML COP displacement, similar results were obtained. McCrory et al. [26] showed that there was no difference in GRF between pregnant women and a CG. ML displacement COP remained unchanged, but pregnant women compensate with an increase in the width of feet to increase stability in the frontal plane. Lymbery and Gilleard [25] showed in their study that the GRF was unaffected by body mass and another study from 2013 analysed the factors that influence the COP in the elderly subject and found that body mass index (BMI) did not influence COP parameters despite the tendency to flat foot in these individuals [19] that pregnant women had too [6]. It can be hypothesised that this observation could be extrapolated to pregnant women.

A significant group effect on PA-ML COP excursion was found (p = 0.009). A decreased COP displacement in pregnant women can thus be advanced as compared to CG. Several factors can explain this effect. At first, the trend to lower ML COP displacement in pregnant women may be related to an increase in foot volume [3], [28]. Foot shape modification can influence COP movement. Flat feet are known to display a different COP excursion compared to rectus feet or cavus feet, COP path is less concave, more medial and, therefore, shorter. However, the correlation between COP trajectory and dynamic foot function is poor (r = 0.43) [24]. Secondly, an enlargement of the base of support [23], [29] was found in late pregnancy, resulting in a lateral COP displacement increased GRF and increase of pressure on the lateral forefoot [25].

The ML plane remains better controlled due to the increase in the base of support [29]. Jang et al. [23] obtained a very good correlation (r = 0.94) between foot width and stability. Reduced COP displacement in AP direction could be linked to the waddling type of gait adopted by pregnant women. Waddling gait is characterized by an increase of support on the metatarsal heads and on the medial part of the hallux at the end of stance phase rather than the entire toe, coupled to an increase in maximum rearfoot pressure, probably as an adaptation to anterior mass increase [17], [25], [28].

COP in postpartum

After childbirth, women maintained a natural walking speed (1.11 \pm 0.14 m/sec) relatively similar to that obtained during pregnancy. Postpartum gait velocity remained slower than that of the CG (by12%). These results confirm those of the study by Forczek and Staszkiewicz [8], [14], which stated that gait parameters returned to pre-pregnancy values within approximately 6 month after delivery, which is the time required to completely restore the mass and dimensions of women. COP parameters returned to CG values (maximal follow-up of 8 months). Lymbery and Gilleard [25] showed that plantar pressures returned to normal 8 weeks and 4 months after childbirth. Even if follow-up duration after childbirth differs between studies, and considering the small size of the PPG in this study, it can be advanced that COP parameters gradually return to normal values together with the decrease in mass and hormonal status.

Intra-variability

The variability was, in general, larger for frontal plane COP parameters compared to the sagittal plane.

These results are consistent with those of Lymbery and Gilleard [25], which suggest that pregnant women establish specific control strategies along the ML axis: ML oscillations are lower because control occurs by an increase of the support base, causing larger intrasubject variability.

Moreover, as previously seen, several authors [11] have shown that greater local stability is correlated with slower walking speed. However, a slower gait leads to greater variability of gait parameters, which implies a deterioration of stability [11]. In spite of lower velocity in PG, low variability in gait parameters as that found in our study, was shown to be correlated with greater stability and a low risk of falling [11]. The CG had a greater variability compared to pregnant women, what was probably related to the increase in base of support strategy used by pregnant women. Our findings may join those of Kadaba et al. [24], which suggest that the pattern of gait is relatively reproducible and intra-variability is excellent at preferred speed. Pregnant women had thus developed optimal strategies for balance. Strategies aiming at improving gait stability in pregnant women are comparable to the ones observed in elderly subjects with pronated feet and lower gait velocity [10]. A study on plantar pressures and footprints of pregnant women would contribute to further clarify the results.

Limitations

Concerning the limitations of our study, the methods of selection of women may have influenced our results since women were recruited during the preand postnatal gymnastic classes. It can be advanced that participation in such classes improves body perception and muscle strength. Furthermore, for organisational reasons, a longitudinal study could not be achieved. It would have reduced the risk of differences between groups other than those related to pregnancy progression. Presently, there is no consensus about the delay needed to restore normality of COP during gait in post-partum. An influence of a previous pregnancy on the results can thus not be excluded. Finally, the small number of subjects in some groups could be a limitation of the study. For these reasons further studies are required.

5. Conclusions

Over the last four months of pregnancy, PG decreased gait velocity but the study showed the absence of COP parameters modification. As compared to CG,

PG had decreased gait velocity, PA and ML COP velocity and PA-ML COP excursion. After delivery, increased gait velocity was found, but it remained lower compared to CG. COP modifications suggests that pregnant women establish specific and individual strategies, potentially related to foot structure changes and support base increase, with the aim of maintaining stability during gait with a lower variability.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this article.

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102

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