

## Foot-floor contact pattern in children and adults with Dravet Syndrome

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### ARTICLE INFO

#### Keywords:

Severe myoclonic epilepsy of infancy (SMEI)

Gait

Pedobarography

Biomechanics

Center of pressure

Heel strike

### ABSTRACT

**Background:** Dravet Syndrome (DS) is a developmental and epileptic encephalopathy characterized by severe drug-resistant seizures and associated with cognitive and motor impairments. Walking problems are frequently observed. As the foot plays a key role during walking, compromised foot function can be a feature of deviant gait.

**Aim:** To investigate foot function in DS by characterizing foot-floor contact patterns using pedobarography.

**Methods:** A total of 31 children and adults were included in the DS group (aged 5.2–32.8 years, 17 female, 174 steps) and 30 in the control group (aged 6.0–32.9, 16 female, 180 steps). The foot-floor contact pattern was evaluated based on progression, length and smoothness (spectral arc length) of the center of pressure (CoP). Linear mixed models were used to identify differences between non-heel strikes and heel strikes and between the DS and control group.

**Results:** Fifteen participants with DS showed inconsistency in the type of foot-floor contact (heel strikes and non-heel strikes). Heel strikes of participants with DS had significantly reduced time of CoP under the hindfoot and increased time under the midfoot region compared to the control group. Significant time and age effects were detected.

**Conclusions and implications:** Deviant foot-floor contact patterns were observed in DS. Possible gait immaturity and instability as well as implications for interventions are discussed.

### 1. Introduction

Dravet Syndrome (DS) is a developmental and epileptic encephalopathy with an estimated prevalence between 1/15000 and 1/40000. In at least 80 % of cases, it is caused by mutations in the gene encoding the sodium channel type I alpha subunit, *SCN1A* [1,2]. The syndrome is characterized by drug resistant infantile onset seizures accompanied by cognitive, behavioral and motor impairments [3,4]. Children with DS show a delay in motor development before the age of two, often with a delayed achievement of independent walking [5–7]. Diverse gait alterations have been described in DS, with about half of the investigated cases presenting a gait pattern which resembles crouch gait [6,8,9].

Although gait problems are a major concern for children and adults with DS and their caregivers [10,11], scarce literature has addressed this topic and especially quantitative assessments of gait deviations are lacking [8].

The foot plays a key role during walking as it supports the weight of the body on the ground. The dynamically functioning foot is required to be sufficiently flexible to provide stability on any surface and at the same time to be a rigid lever able to transmit propulsive forces for an efficient walking pattern [12]. Detailed evaluation of foot function is possible using three dimensional motion analysis with multi-segment foot models [13–15]. However, this procedure requires high levels of participant collaboration, which makes it a less feasible option in DS due

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to cognitive and behavioral problems. Less complex approaches such as pedobarography may provide meaningful insight into foot function. In pedobarography, pressure platforms are used to analyze the pressure distribution under the foot. Quantitative measures enable the objective detection of disturbed foot-floor contact patterns [16].

A relevant plantar pressure measure is the center of pressure (CoP) and its trajectory on the plantar surface, also referred to as 'gait line'. The CoP is defined as the centroid of all external forces acting on the plantar surface of the foot and is often used as an indirect measure of neuromuscular control [17,18]. A mature foot-floor contact pattern is characterized by a heel strike at initial contact followed by a fluent movement of the CoP from the medial aspect of the heel over the lateral side of the foot, ending with a quick medial shift on the forefoot. Impaired motor control may affect the ability to consistently perform heel strikes. Deviations in CoP trajectories may reflect compromised foot function and pathological gait [18]. This study aims to investigate foot function in children and adults with DS by characterizing foot-floor contact patterns using pedobarography. We hypothesize that differences in progression, length and smoothness of the CoP trajectory can be detected between patients with DS who consistently perform heel strikes, those who are not able to consistently perform heel strikes and able-bodied controls.

## 2. Methods

### 2.1. Setting

Data collection was performed at the Laboratory of Clinical Analysis and Biomechanics of Movement and Posture, University Hospital of Padua, Italy. Patients with DS were recruited at Neurological Institute Carlo Besta, Milan, Italy, University Hospital of Padua, Italy and Verona University Hospital, Verona, Italy. Measurements took place between May 2015 and October 2019. The study was approved by the Ethical Committee of the Padua University Hospital (protocol number 4276/AO/17).

### 2.2. Inclusion

All participants with a minimum age of five years and a genetically confirmed diagnosis of DS were eligible. Exclusion criteria were the inability to walk without assistance, or the occurrence of a convulsive seizure within 24 h prior to the examination. Age-matched able-bodied volunteers were enrolled as control group. Exclusion criteria for the control group were a history of neurological or orthopedic disorders. All participants and their legal guardians provided written informed consent.

### 2.3. Data collection

Height, weight and foot length (from the most proximal apex of calcaneus to the most distal apex of the toes) were measured and inspection of the foot posture in stance was performed. Pedobarographic data were collected using the midgait method [19] on a walkway with an embedded plantar pressure platform (100 Hz, 4 sensors/cm<sup>2</sup>, from 10 to 12720 kPa, 47.5 × 32.0 cm<sup>2</sup>, max force: 193 kN, emed-q®, Novel GmbH, Munich, Germany). Participants walked barefoot at self-selected walking velocity and were instructed not to look down or target the pressure mat. As long as participant cooperation was ensured, trials were repeated until at least six successful steps per side were collected. In case participants were less cooperative, only the side(s) with a minimum of three successful steps were included. Due to behavioral issues, all 'clean' steps on the platform were collected, even steps that were less representative for the participant's usual gait pattern. Afterwards, steps considered most representative were identified in a standardized manner. Hereto, custom made MATLAB® scripts (R2018a, The Mathworks Inc, Natick, MA, US) were used to calculate correlations between

all pressure distribution images within each participant (Appendix A). For each side, the three footprints with the highest correlation among each other were selected for further analysis.

### 2.4. Processing

The longitudinal axis of the foot was determined as the bisect between the tangents for the medial and lateral sides of the maximum pressure picture. Three regions were identified based on two lines perpendicular to the longitudinal axis as defined in the platform's standard software: one at 27 % of the heel-toe distance to separate hindfoot and midfoot, and one at 55 % to separate midfoot and forefoot (Fig. 1c). The toes were included in the forefoot region (Multimask v23 Novel GmbH, Munich, Germany). Manual quality control assured correct masking and confirmed that all included steps were full footprints. The CoP was determined as the weighted centroid of the total number of active sensors for each data sample. Based on the region where the first CoP point was situated, steps were identified as heel strikes (hindfoot) or non-heel strikes (mid- or forefoot region). A low pass fourth order Butterworth filter at 20 Hz was applied to the CoP trajectory over time, using a reflection technique to avoid edge effects at the beginning and end of the signal [20]. After filtering, six parameters were calculated as presented in Table 1. Filtering and parameter calculations were implemented in MATLAB®.

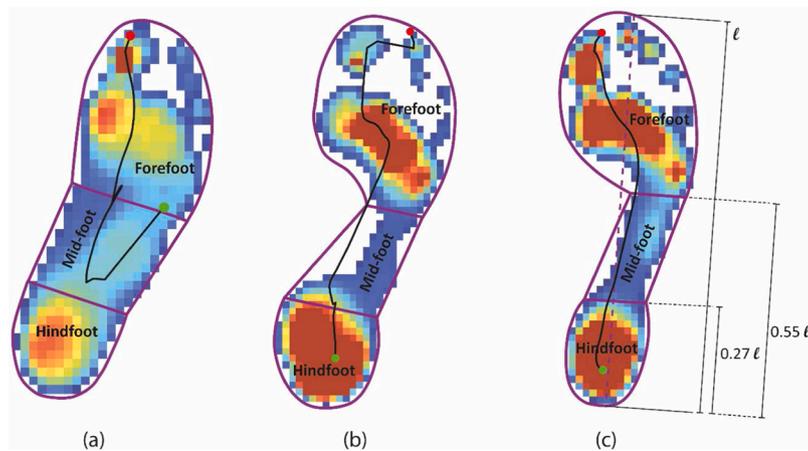
The CoP progression (CoPP) was calculated for the three foot regions as the time during which CoP was situated under that region relative to total contact time (TCT). Length ratio was defined as the CoP trajectory path length normalized by clinically measured foot length. Mature foot-floor contact patterns were expected to have a length ratio of approximately one, with larger values indicating less efficient gait due to additional or compensatory movements. Smoothness of the CoP trajectory was assessed by calculating the spectral arc length (SPARC), the arc length of the Fourier magnitude spectrum within an adaptive frequency range. This smoothness index proved to be sensitive, robust to measurement noise and independent of temporal movement scaling [21]. SPARC was calculated for the medio-lateral (M-L SPARC) and antero-posterior (A-P SPARC) components of the CoP displacement vector, using code provided by Balasubramanian et al. (2015) [21]. SPARC is a negative number with larger absolute values indicating more interruptions and thus less smooth CoP trajectories.

### 2.5. Statistical analysis

Descriptive statistics were computed for demographics and step characteristics. The demographic data were compared between groups using Mann-Whitney U tests, after Shapiro-Wilk tests did not confirm a normal distribution.

Non-heel strikes were only observed in the DS group and resulted in v-shaped CoP trajectories (Fig. 1a). Because of this different shape, it would not have been appropriate to compare them with heel strikes from the control group. We therefore used a two-stage approach. In the first stage, the effect of the type of initial contact on CoP parameters was analyzed within the DS group and non-heel strikes were omitted in stage two. In the second stage, distinction was made between participants with DS that always performed heel strikes and those who inconsistently switched between non-heel strikes and heel strikes. Comparison of CoP parameters was then performed between the two DS subgroups ('DS\_consistent' and 'DS\_inconsistent') and the control group.

Linear mixed models were fitted to assess the effect of the type of initial contact (non-heel strike or heel strike) and group (DS\_consistent, DS\_inconsistent or control) respectively, on the main outcome parameters. Age, TCT and side (left, right) were added as fixed effects. To account for non-independence of observations, subject and side, nested within subject, were entered as random effects. Significance of the fixed effects was tested using a likelihood ratio test. We first fitted linear mixed models testing the effect of type of initial contact on each of the



**Fig. 1.** Example images of center of pressure trajectories on maximal pressure images of a) non-heel strike by a participant with DS, b) heel strike by a participant with DS and c) heel strike by a typically developing volunteer. Purple lines indicates the applied masking to identify the hind-, mid- and forefoot regions, with those being separated by two lines perpendicular to the longitudinal axis of the footprint (purple dashed line in (c): one at 27 % of the heel-toe distance ( $l$ ) to separate hindfoot and mid-foot; and one at 55 % to separate midfoot and forefoot (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).

**Table 1**  
Definition of the main outcome variables.

CoP trajectory	Parameter	Definition
<b>Progression</b>	CoPP hindfoot	CoP progression on hindfoot (% of total contact time)
	CoPP midfoot	CoP progression on midfoot (% of total contact time)
	CoPP forefoot	CoP progression on forefoot (% of total contact time)
<b>Length</b>	Length Ratio	CoP trajectory path length (cm) / foot length (cm)
<b>Smoothness</b>	M-L SPARC	Medio – lateral spectral arc length
	A-P SPARC	Antero – posterior spectral arc length

CoPP, center of pressure progression; CoP, center of pressure; SPARC, Spectral arc length; M-L, medio-lateral; A-P, antero-posterior.

six outcome measures within the DS group. Subsequently, we fitted linear mixed models to detect differences between the DS subgroups and control group for all outcome parameters. If the existence of a significant difference was revealed, post hoc pairwise comparisons (Bonferroni) using estimated marginal means, were performed to detect differences between groups. All statistical analyses were performed in R (v 4.0.0, R Foundation, Vienna, Austria, packages ‘lme4’ and ‘emmeans’) [22]. Details on the linear mixed models analysis can be found in Appendix B.

The nominal significance level was set at  $P < .05$ , but may not be appropriate as a cut-off for the linear mixed models, because multiple hypotheses were tested. Since there were moderate correlations between the six outcomes, a Bonferroni correction would be too conservative. A Benjamini-Hochberg correction, controlling for a false discovery rate of 0.05, was applied to interpret the results of the linear mixed models [23].

### 3. Results

#### 3.1. Demographics and step characteristics

In total, 31 children and adults with DS (174 steps) and 30 age-matched typically developing volunteers (180 steps) with an age range from 5.2 to 32.9 years were included in the study (Table 2). Out of 46 eligible candidates with DS, 15 patients needed to hold hands for guidance or support, could not repeat trials until a sufficient number of steps were collected or did not walk in a straight line in a representative manner and were thus excluded. Among the 31 participants with DS, 17 had planovalgus feet (pronation) and four hindfoot varus (supination), of whom 12 wore insoles with arch and hindfoot support or orthopedic shoes (Table 2).

Out of a total of 174 steps in the DS group, 139 (80 %) were heel

**Table 2**  
Demographics per group and subgroup.

Demographics	DS			Control (n = 30)
	Total (n = 31)	DS_consistent subgroup (n = 15)	DS_inconsistent subgroup (n = 16)	
Age (year)	13.0 (5.2; 32.8)	15.1 (6.9;32.8) *	11.1 (5.2;24.6)*	13.5 (6.0; 32.9)
Gender (male/female)	14 / 17	7 / 8	7 / 9	14 / 16
Height (cm)	147.0 (106.0; 194.5)	155.5 (119.5; 194.5)*	139.8 (106.0;164.0)*	160.5 (117.0; 180.5)
Weight (kg)	42.0 (18.5; 83.5)	51.0 (20.0; 83.5)	35.0 (18.5; 69.5)	48.5 (19.5; 81.5)
Foot morphology (n):				
Pronation (planovalgus)	17	6	11	
Supination (varus)	4	3	1	
Neutral	10	6	4	
Insoles or orthopedic shoes (n)	12	5	7	

Median (min; max).

\* Significant difference between DS subgroups. DS, Dravet Syndrome; n, number of participants.

strikes and 34 (20 %) were non-heel strikes (eight with first CoP on the midfoot region and 27 on the forefoot region). The non-heel strikes were observed in 16 participants with DS of which one always performed forefoot strikes while the others varied with heel strikes. These 16 participants formed the DS\_inconsistent subgroup with a median age of 11.1 years (range 5.2–24.6 years). The 15 participants with DS who always performed heel strikes, formed the DS\_consistent subgroup with a median age of 15.1 years (range 6.9–32.8 years). The DS\_inconsistent subgroup was significantly younger ( $P = .03$ ) with lower height ( $P = .03$ ) than the DS\_consistent subgroup.

#### 3.2. Stage 1: Comparison of non-heel strikes with heel strikes within participants with DS

Linear mixed models compared heel strikes with non-heel strikes within the DS group, accounting for age and total contact time (TCT). The likelihood ratio test ( $\chi^2$ ) revealed a significant difference between the two types of initial contact for all parameters except CoPP midfoot

and M-L SPARC. When controlling for age and TCT, the CoPP hindfoot was significantly shorter ( $P < .001$ ), while CoPP forefoot was longer ( $P < .001$ ) in case of a non-heel strike, with increased Length Ratio ( $P < .001$ ) and decreased smoothness on A-P SPARC ( $P < .001$ ; Fig. 2). Detailed statistical output is reported in Appendix B.

One outlier with a length ratio of 2.50 was observed among the non-heel strikes in the DS group. This outlier did not alter the conclusions on the effect of type of initial contact.

### 3.3. Stage 2: Comparison of heel strikes between DS subgroups and typically developing volunteers

When comparing heel strikes between the DS subgroups and control group, accounting for TCT and age, the likelihood ratio test ( $\chi^2$ ) detected a significant difference for CoPP hindfoot ( $P = .002$ ) and CoPP midfoot ( $P < .001$ ). Post hoc pairwise comparison revealed decreased CoPP hindfoot ( $P = .003$ ) and increased CoPP midfoot ( $P < .001$ ) in the DS\_inconsistent subgroup compared controls. Other parameters did not differ significantly (Fig. 2). Detailed statistical output is reported in Appendix B.

### 3.4. Relation with TCT and age

In addition to group effects, the linear mixed models investigated the effects of TCT and age on the different CoP trajectory parameters. In stage1, TCT had a significant effect on all CoP trajectory parameters, while age did not show any significant effect. With increasing TCT, an increase of CoPP hindfoot ( $P = .03$ ), CoPP midfoot ( $P = .002$ ) and Length Ratio ( $P = .03$ ) was observed and a decrease of CoPP forefoot ( $P < .001$ ), M-L SPARC ( $P < .001$ ) and A-P SPARC ( $P < .001$ ). In stage 2, significant effects of age and TCT were observed. With increasing TCT, CoPP midfoot slightly increased and CoPP forefoot, M-L SPARC and A-P SPARC decreased (all  $P < .001$ ). Small but significant age effects revealed decreased CoPP hindfoot ( $P = .04$ ), increased CoPP forefoot ( $P = .01$ ) and reduced M-L SPARC ( $P < .001$ ) with increasing age. Details on linear mixed models and the resulting regression equations can be found in Appendix B.

## 4. Discussion

This study aimed to investigate foot function by characterizing the

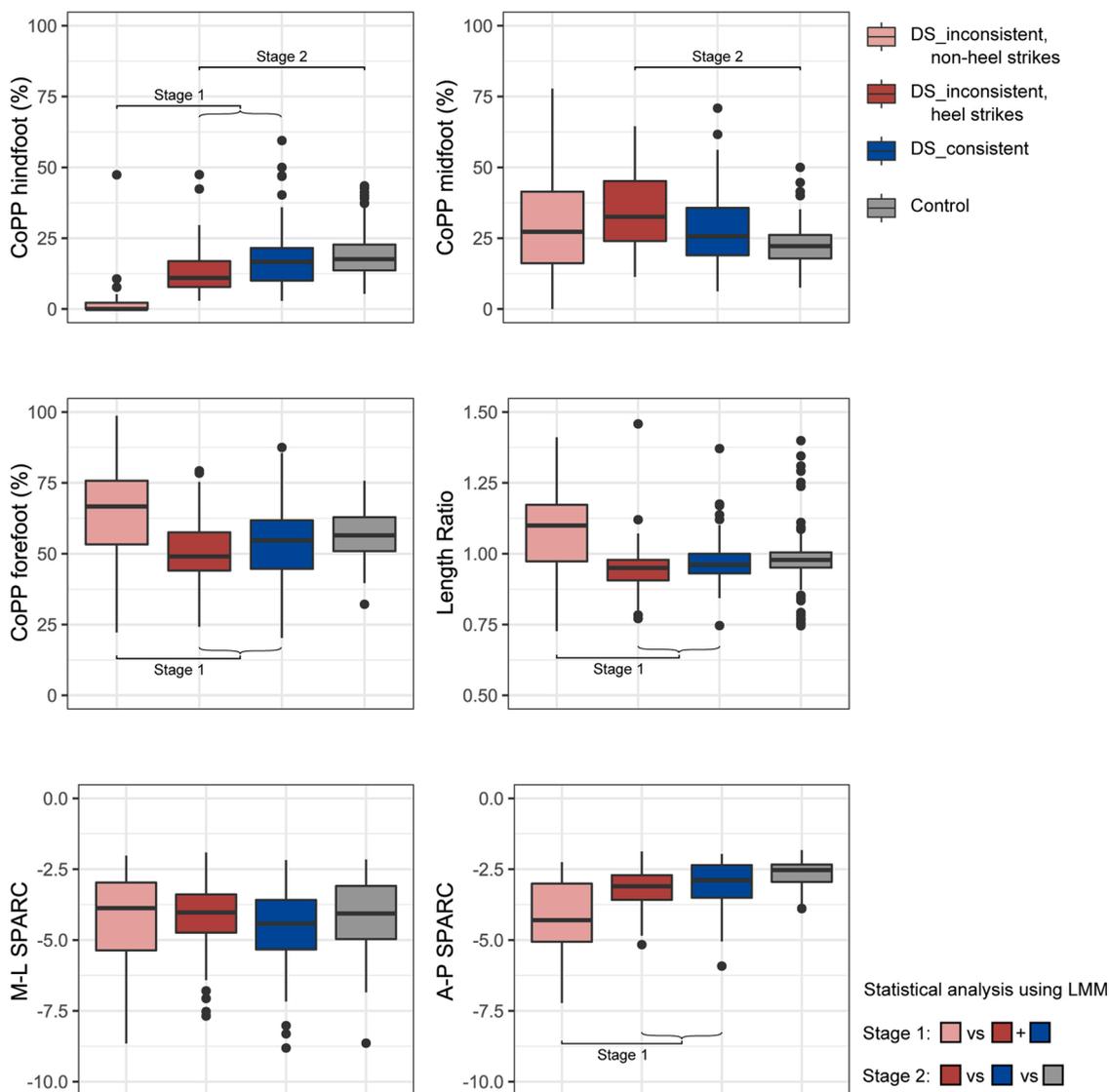


Fig. 2. CoP trajectory parameters per (sub)group with subdivision of heel strikes and non-heel strikes. Significant differences were detected using linear mixed models (LMM) controlling for age and total contact time in two stages: between non-heel strikes and heel strikes within DS (Stage 1) and between heel strikes of DS\_inconsistent, DS\_consistent and control group (Stage 2). DS, Dravet Syndrome; CoPP, center of pressure progression; SPARC, Spectral arc length; M-L, medio-lateral; A-P, antero-posterior.

foot-floor contact pattern in a group of people with DS compared to a group of typically developing children and able-bodied adults. Six parameters were selected to evaluate the progression, length and smoothness of the CoP trajectories on the plantar surface of the foot. About half of the participants with DS did not consistently initiate their step with a heel strike. The relative duration of CoP progression in non-heel strikes was larger on the forefoot and lower on the hindfoot, as was expected since most of the non-heel strikes were forefoot strikes. The typically v-shaped CoP trajectory of these non-heel strikes was reflected in longer path lengths and decreased antero-posterior smoothness. The DS\_inconsistent subgroup also showed deviant CoP trajectories when only heel strikes were compared with DS\_consistent and control group. More specifically, the CoP progression significantly differed, revealing a quick transition of the CoP from hind- to midfoot region in DS\_inconsistent. Contrary to our hypothesis, DS participants did not perform heel strikes with different path lengths or smoothness compared to the control group. These results showed that the foot-floor contact pattern was significantly different in patients who were unable to consistently perform heel strikes. Patients with impaired foot function can be distinguished based on foot strike pattern and deviant CoP trajectories.

In previous research on typically developing children, mid- and forefoot strikes have been frequently observed early after the onset of independent walking. The foot strike patterns normalized to heel strikes during the first year of walking experience and the gait line appeared smoother with increasing age [24–26]. In DS, not only a later onset of independent walking but also a persisting delay in overall motor development is observed [5], which could contribute to immature foot strike patterns. These observations might indicate immaturity of gait in children and adults with DS. This hypothesis is supported by the findings of significant age effects on CoP trajectory parameters and younger age in the DS\_inconsistent group.

Even when participants with DS did perform heel strikes, it is likely that increased time during which CoP was situated on the midfoot (increased CoPP midfoot) bears the functional significance of a quest for more stability or may reflect altered muscle function. Stability issues during gait are in line with previous research suggesting that atypical crouch gait and increased step width were compensation strategies to increase stability by lowering the center of mass and widening the base of support [9]. Impaired motor control or muscle strength may cause the incapacity to slow down the forward motion of the tibia [27] which would result in a quick transition of the CoP from hind- to midfoot. This may be reflected in kinematic deviations previously described in this population, specifically early and increased ankle dorsiflexion [9] and might contribute to crouch gait [6,9,27]. Pathophysiologic findings in DS suggest that motor control is often disturbed owing to central nervous disorders [28,29] and possibly peripheral neuropathy [7]. Clear muscle weakness is not reported, but studies evaluating strength are lacking [6]. Future studies should investigate the link between CoP progression, clinical findings and the gait pattern.

Besides stability, strength or control issues, also malalignment of the foot may affect the excursion of the CoP [17]. Deviating static foot postures were observed in 65 % of the participants with DS, mostly pronated feet (planovalgus). Foot morphology could directly affect the CoP trajectory and may also be linked to abnormal foot strike patterns, as 77 % of the participants with pronated feet also performed non-heel strikes. Further investigation of the dynamic behavior of these deviations during gait and the influence of supportive footwear is needed to clarify how foot morphology may contribute to gait deviations in children and adolescents with DS.

For in depth investigation of the link between CoP trajectories and the gait pattern, additional video or three dimensional gait analysis (3DGA) is required. This combination proved to be more accurate to identify regions of the foot [30] and to detect the absence of a heel strike [31]. Furthermore, 3DGA provides essential information on gait patterns and should ideally be performed to assess gait in patients with DS. However, even better participant collaboration is needed to collect

reliable 3DGA data and it requires advanced motion capture infrastructure [32]. Hence, when 3DGA proves too demanding in participants with severe cognitive and behavioral impairments, pedobarography combined with video analysis may offer a feasible alternative. The CoP trajectory may then provide insight into foot function and mechanical control to enable integrated interpretation of observed gait deviations [18].

The results imply that people with DS may benefit from interventions that improve foot-floor contact patterns and provide stability in order to walk with a more efficient pattern. Physiotherapy with an emphasis on practicing correct foot strike patterns and improving plantar flexor muscle function could be indicated. Shoes could provide stability around ankle and foot, especially in combination with orthopedic insoles in case of foot deformities.

Cognitive and behavioral impairments in people with DS were a limiting factor that could impact the generalizability of the results. Out of 46 eligible candidates, 15 were excluded because the minimum of three representative steps for one side was not reached owing to behavioral or cognitive limitations. It remains unclear whether these participants' foot-floor contact patterns were similar to the included participants with DS or if their exclusion resulted in an underrepresentation of severely affected patients in this study.

#### 4.1. Conclusion

Half of the participants with DS showed inconsistency in the type of foot-floor contact (heel strikes and non-heel strikes). Even when participants in this subgroup performed heel strikes, their CoP progression pattern differed from typically developing controls, more specifically by a reduced duration of CoP under the heel and a prolonged duration under the midfoot.

#### Funding

This study was supported by Dravet Italia ONLUS (Associazione Italiana Sindrome di Dravet Onlus) and YouReCa KU Leuven. The funding source was not involved in the study process and article submission.

#### Declaration of Competing Interest

The authors report no declarations of interest.

#### Acknowledgements

The authors thank the participants and their families for their cooperation and Dr. Erik Fransen for his statistical expertise. This study was supported by Dravet Italia ONLUS (Associazione Italiana Sindrome di Dravet Onlus), Gruppo Famiglie Dravet, and YouReCa KU Leuven.

#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.gaitpost.2020.12.030>.

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