The fractal dimension approach in posture: a comparison between Down and Prader–Willi syndrome patients

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1. Introduction

Prader-Willi syndrome (PWS) and Down syndrome (DS) are two different chromosomal disorders characterised by some common clinical features, such as obesity, muscular hypotonia, ligament laxity and mental retardation. Their ability to sit, kneel, stand and walk is compared with the ability of children of the same age, and in adult life, although hypotonia does not progress, the progressive effects of obesity on joints produce a cautious abnormal gait and posture (Davis and Kelso 1982; Butler 2006; Goeltz 2006; Cimolin, Galli, Grugni, et al. 2011). Since balance is a key function for performing daily life tasks, investigating this capacity appears necessary to define the functional profile in the PWS and DS population to be able to plan appropriate rehabilitation interventions.

In general, the integrity of the postural control system is evaluated by analysing the centre of pressure (CoP) with static posturography. The effectiveness of the postural control system has been related to the magnitude of displacements of the CoP, whereas parameters related to the velocity of CoP are generally associated with posturographic activity to achieve this level of stability (Myklebust et al. 1995). Postural control is often assessed as a variation in the ground reaction forces during quite standing and generally the analysis of the application point of the resultants of these forces, the CoP, is conducted as a function of time. However, from a physiological point of view, the information obtained by the common CoP time-domain analysis cannot be univocally interpreted. The CoP represents in fact the sum of various neuro-musculoskeletal components acting at different joint levels and its time series is two dimensional or planar. Although the two components of the signal, anteriorposterior and mediolateral, are generally analysed separately, they represent the output of a unique integrated system. In addition, posture can be considered to be a dynamic stability of a continuously moving body. For this reason, human movement is not separated into a perfect static state (posture) and a dynamic state (movement), as posture and movement could be considered to be adaptively and flexibility integrated. As a consequence, the utility of static posturography in clinical practice needs for reliable approaches in order to extract physiologically meaningful information from stabilograms (Myklebust et al. 1995; Manabe et al. 2001). During the last decades, various new mathematical tools have been used to better characterise the nonlinear and dynamic features of postural variability. Among these methods, the fractal dimension (FD) approach has been proposed in order to better describe the dynamic patterns of biological signals (Myklebust et al.

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Table 1. Characteristics of the study groups.

	PWS	DS	OCG	HCG
Participants (M/F)	13 (6/7)	20 (11/9)	26 (15/11)	20 (10/10)
Age (years)	32.4 ± 4.2	29.1 ± 8.1	34.2 ± 10.7	31.4 ± 9.6
Height (m)	1.52 ± 0.8*, **	1.51 ± 0.1*, **	1.67 ± 0.9	1.73 ± 0.5
BMI (kg/m^2)	40.3 ± 6.6*	35.8 ± 6.2*	40.6 ± 4.6*	22.8 ± 3.2
Foot length (mm)	209.6 ± 13.1*	219.8 ± 14.7*	222.5 ± 10.1*	239.9 ± 11.4

Notes: PWS, Prader–Willi syndrome; DS, Down syndrome; OCG, healthy control group; HCG, healthy control group. Data are expressed as median and quartile range. *$p < 0.05$, compared with HCG; **$p < 0.05$, compared with OCG.

1995; Peng et al. 2000; Manabe et al. 2001; Doyle et al. 2005), representing a relative measure of the number of elemental units fabricating a pattern. Previous studies (Myklebust et al. 1995; Manabe et al. 2001; Doyle et al. 2005) have demonstrated that fractal analysis represents a reliable method to highlight specific characteristics of balance control. FD can in fact be used to quantify the complexity of CoP trajectory: a change in FD may indicate a change in control strategies for maintaining quiet stance and in the stability of the system: the higher FD, the more complex the CoP signal (Doyle et al. 2005). In literature, only few studies have been conducted using the FD technique to investigate posture and they were conducted on Parkinson and ataxia (Manabe et al. 2001), on PWS (Cimolin, Galli, Rigoldi, et al. 2011) and on DS patients (Rigoldi et al. 2012). The authors found FD to be more sensitive in the evaluation of postural instability in these conditions than the traditional stabilometric analysis conducted using time-domain analysis.

According to the need for a deeper investigation of postural instability in DS and PWS and to the promising application of an FD approach on PWS patients, our goal was to quantitatively compare postural control in adult PWS and DS, not only considering the traditional methods of CoP analysis in time-domain, but also using the frequency-domain technique and the FD approach, in order to evaluate if these methods could offer additional and clinically useful information.

The main limitation of previous studies on PWS and DS was that they compared results to a normal weight control group, without taking in consideration the possible influence of obesity on postural ability. There is evidence that body weight is a strong predictor of postural stability (Hue et al. 2007), with obesity-associated postural perturbations appearing in adolescence (McGraw et al. 2000). In particular, obesity has been associated with greater forward displacement of the CoP during dynamic standing balance activities (Berrigan et al. 2006). Based on such considerations, we included also a control group composed of healthy obese individuals.

2. Methods

2.1 Participants

In this study, we enrolled 20 DS and 13 PWS adult patients matched for age, height and body mass index (BMI; kg/m^2) (Table 1); some of these patients were previously included in another study (Cimolin, Galli, Grugni, et al. 2011). DS patients were all referred to the IRCCS 'San Raffaele Pisana', Tosinvest Sanità, Roma, Italy. The distribution of chromosomal anomalies is pure trisomy 21 in all of the DS patients. PWS patients had been periodically hospitalised at the San Giuseppe Hospital, Istituto Auxologico Italiano, Piancavallo (VB), Italy. All patients showed the typical PWS clinical phenotype (Holm et al. 1993). Cytogenetic analysis was carried out in all participants; 10 had interstitial deletion of the proximal long arm of chromosome 15 (del15q11–q13). Moreover, uniparental maternal disomy for chromosome 15 (UPD15) was found in three subjects.

All DS and PWS subjects showed mild mental retardation but were able to understand and complete the test. All participants had to be able to maintain their equilibrium independently without assistance or with the use of crutches, walkers or braces. They were sedentary people and they did not typically take part in sports activities.

Two different groups of subjects were specifically recruited for this study and served as controls (Table 1). The first group included 26 obese subjects (obese control group, OCG), and the second group included 20 healthy subjects with a BMI ranging from 19.3 to 25.4 (healthy control group, HCG). All PWS and control obese patients were found with normal values in main laboratory tests, including adrenal and thyroid function. Exclusion criteria for HCG included prior history of cardiovascular, neurological or musculoskeletal disorders.

All participants were free from conditions associated with impaired balance and individuals with vision loss/alteration, vestibular impairments, neuropathy, as detected by the clinical examination and those who reported symptoms related to intracranial hypertension, were excluded. The study was approved by the Ethics Committees of the two Institutes for DS, PWS patients and OCG, respectively. Written informed consent was

obtained by the parents or, when applicable, by the patients.

2.2 Experimental set-up

Static posturography was conducted on a non-movable force plate (Kistler, CH; acquisition frequency: 500 Hz). The participants were asked to stand for 30 s on the force platform, their feet placed with an angle of 30° in a fixed and standardised position and their arms at their sides. The individuals were instructed to maintain normal standing balance, undisturbed stance with eyes opened looking at a black target 1.5 m far away (a circle with a diameter of 6 cm) which was positioned vertically to be in the patient's direct line of sight, in order to standardise the trials. For each subject, a sequence of three trials was carried out at 10-min intervals, in order to minimise the possibly confounding effect of fatigue.

2.3 Data analysis

The outputs of the force platform allowed us to compute the CoP time series in the A/P direction (CoPAP) and the M/L direction (CoPML). The output of the platform was processed to compute quantitative parameters in time domain and frequency domain as well as using the FD technique. The computed parameters computed as for time-domain and frequency-domain analyses were listed in Table 2.

All the parameters computed using the time-domain analysis were normalised to the participant's height (expressed in metres) and to their foot length (expressed in millimetres). In fact, short feet are one of the typical features of PWS (Hudgins and Cassidy 1991) and DS patients (Diamond et al. 1981). It has been shown that the base of support, as calculated from the foot length, is one of the most relevant biomechanical variables in the postural analysis (Chiari et al. 2002).

As for FD parameter, it was computed on the image of CoP trajectory using the box-counting method (Feder 1988). Briefly, let us superimpose a square grid on the image, being ε the edge size of each square, and let us indicate as $N(\varepsilon)$ the number of squares needed to fully cover the image. It can be shown that, in the limit $\varepsilon \rightarrow 0$, we have

$$N(\varepsilon) \sim \frac{1}{\varepsilon^D}, \tag{1}$$

where D is known a box-counting FD. The quantity D can be estimated by computing $N(\varepsilon)$ for different values of grid size ε. According to relation (1), this yields an array of points in log–log space that can be fitted with a straight line whose negative slope provides an estimate of the FD value. This parameter allows estimating the stabilometry pattern more quantitatively than the traditional methods. A signal with an FD equal to 1 would indicate a completely stationary signal over time, whereas an FD of 2 would indicate a signal that oscillates equally about a central tendency over time. This value is higher when the picture is more complex. In particular, this method allows the bi-dimensional analysis, not used in the previous studies which generally used FD approach in one dimension (for postural analysis in the anterioposterior and mediolateral directions, separately) (Blaszczky and Klonowsky 2001; Manabe et al. 2001; Doyle et al. 2005).

2.4 Statistical analysis

All the previously defined parameters were computed for each participant and then the median and quartile range values of all indexes were calculated for each group. Kolmogorov–Smirnov tests were used to verify if the parameters were normally distributed; the parameters were not normally distributed, so we used analysis of

Table 2. Descriptors of the parameters computed from time-domain and frequency-domain analyses of CoP.

Parameters computed from time-domain and frequency-domain analyses	
Time-domain parameters [a]	
RANGEAP and RANGEML (1/m)	The range of CoP displacement in the A/P direction (RANGEAP index) and the M/L direction (RANGEML index), expressed in mm and normalised to subjects' height (m) and foot length (mm)
Sway path (SP) (1/m)	The total CoP trajectory length, expressed in mm and normalised to subjects' height (m) and foot length (mm)
Frequency-domain analysis [b]	
fML and fAP	The centre frequency of the main spectral peak of the P spectrum in mediolateral (fML index) and anteroposterior direction (fAP index)

[a]The anteroposterior and mediolateral coordinates of the CoP trajectory underwent a post-acquisition filtering using a low-pass filter with a cut-off frequency of 10 Hz (Schmidt et al. 2002).
[b]The signals were first down-sampled (anti-aliasing filter) at 10 Hz. The analysis was performed using parametric estimators based on autoregressive (AR) modelling of the data (Galli et al. 2008).

Table 3. Postural parameters of the study groups.

	PWS	DS	OCG	HCG
Time-domain parameters				
RANGEAP (1/m)	0.06 (0.03)$^{+}$, *, **	0.05 (0.02)*, **	0.03 (0.01)*	0.02 (0.01)
RANGEML (1/m)	0.07 (0.02)*, **	0.06 (0.02)*, **	0.03 (0.01)	0.03 (0.02)
SP (1/m)	2.79 (0.89)$^{+}$, *, **	4.29 (0.82)*, **	0.72 (0.86)	0.51 (0.98)
Frequency-domain parameters				
fAP (Hz)	0.10 (0.09)$^{+}$	0.31 (0.23)*, **	0.10 (0.09)	0.16 (0.16)
fML (Hz)	0.13 (0.12)$^{+}$	0.22 (0.18)*	0.19 (0.14)	0.12 (0.15)

Notes: PWS, Prader–Willi Syndrome; DS, Down syndrome; OCG, obese control group; HCG, healthy control group. Data are expressed as median and quartile range. The values of time-domain parameters are normalised for the subject's height and foot length. $^{+}p < 0.05$, PWS group versus DS group; $*p < 0.05$, compared with HCG; $**p < 0.05$, compared with OCG.

variance for non-parametric (Kruskal–Wallis) data followed by a *post hoc* range analysis. *P*-Values less than 0.05 were considered significant.

3. Results

In Table 1, the clinical characteristics of DS, PWS, OCG and HCG are reported. Age was not significantly different among groups. BMI, weight and foot length were similar in DS, PWS and OCG, but significantly different when compared to HCG. The height was similar between PWS and DS participants and lower in comparison with OCG and HCG.

Although our first aim was to acquire at least three trials for each participant, the presence of alert state and the decreased cooperation and concentration in our patients did not allow acquiring them in all individuals; for this reason, the data presented were computed starting from the first trial of each patient.

The data obtained using time-domain parameters confirmed previous findings as for the comparison between PWS and DS (Cimolin, Galli, Grugni, et al. 2011). Both DS and PWS individuals showed greater displacements along both the anteroposterior and mediolateral directions (RANGEAP and RANGEML) and longer sway path (SP) parameter when compared to HCG and OCG (Table 3). In particular, PWS and DS were statistically different in terms of RANGEAP and SP parameters, and no alterations were found in terms of RANGEML. HCG and OCG were characterised by similar values ($p > 0.05$).

The frequency-domain analysis showed that while PWS were similar to all healthy participants (to both OCF and HCG), the DS evidenced higher value both in anteroposterior (fAP parameter) and mediolateral (fML parameter) directions when compared to PWS and the two control groups. These results showed that while PWS, OCG and HCG use the same frequency in posture maintenance, the DS used higher frequency in all directions (Table 3).

FD parameter evidenced that both DS and PWS were characterised by greater values in comparison with OCG and HCG, with DS showing higher values than PWS. OCG and HCG displayed a signal with an FD close to 1, with no statistical differences; on the contrary, DS and PWS were characterised by higher FD values, indicating a more complex and irregular signal over time (Figure 1), more accentuated in DS ($p < 0.05$, in the comparison between PWS and DS).

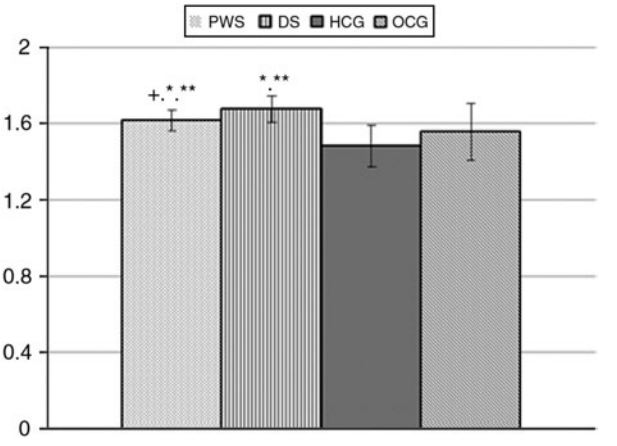

Figure 1. Median (quartile range) of FD parameters for the study groups (PWS, Prader–Willi syndrome; DS, Down syndrome; OCG, obese control group; HCG, healthy control group). $^{+}p < 0.05$, PWS group versus DS group; $*p < 0.05$, compared with HCG; $**p < 0.05$, compared with OCG.

4. Discussion

This comparative study quantified postural parameters in patients affected by DS and PWS, integrating a traditional method (time-domain analysis) with the frequency domain and FD technique. Our aim was to ascertain whether these relatively new approaches would add relevant clinical information to the traditional approach. The characterisation of postural capacity appears a key element for depicting the functional profile of these populations, who yield reduced balance and greater risk of fall than healthy individuals (Finlayson et al. 2010) increased in presence of

obesity (Fjeldstad et al. 2008; Menegoni et al. 2009). The literature on this topic is focused mainly on the data analysis using the time-domain method, and few clinical applications are present (Manabe et al. 2001; Cimolin, Galli, Rigoldi, et al. 2011; Rigoldi et al. 2012) using the frequency-domain and FD technique. In addition, the studies conducted on PWS and DS with traditional techniques did not take into consideration the effect of obesity on postural control, as generally the comparisons were conducted versus normal weight control group and not obese individuals.

Our results are in line with previous studies using the time-domain analysis (range of sway in AP and ML directions and the total trajectory length): PWS and DS showed a higher range of oscillations in both AP and ML directions than HCG and OCG, suggesting generally poorer balance. PWS and DS differed only in AP displacement, lower in DS and higher in PWS, with significant disparities in the length of CoP displacement, higher in DS when compared with those in PWS. The lower value of CoPAP oscillations in DS may be related to their higher hip stiffness as compared to PWS. Interestingly, even if DS showed CoP oscillations close to PWS in the ML direction and lower in AP, their CoP trajectory length was significantly higher than PWS. We can, therefore, hypothesise that the two syndromes are characterised by different CoP velocities, faster in DS than PWS. This hypothesis was confirmed by the frequency-domain approach, which demonstrated that DS was characterised by higher frequency in the two directions. Our results showed, in fact, that although PWS patients showed frequency parameters close to OCG and HCG, DS were characterised by values of frequency higher than the other groups considered in this analysis. This result is in line with the literature on postural control in DS individuals (Galli et al. 2008).

As for the FD parameters, our results showed that both DS and PWS were characterised by higher values than OCG and HCG, with DS higher than PWS. As the nonlinear approach used to compute FD takes into account the dynamic of the signal, these values are indicators of the complexity of the stabilometric pattern in postural maintenance in these individuals, with DS showing a more complex and irregular signal. The higher FD values in our patients may also be interpreted as an inability to synergically modulate the three systems (i.e. visual, vestibular and somatosensory) involved in maintaining posture. Our body is consistently exposed to external perturbations, which we try to counteract by integrating the real-time inputs and the prediction system based on previous inputs. The information given by the nonlinear approach can well describe this mechanism and our data reflect the difficulties encountered by our patients, and particularly accentuated in DS, in adapting to this process. We can assume that these difficulties may be related also to the different cognitive profiles of these two syndromes. PWS patients are, in fact, generally characterised by mild cognitive limitations (Dykens et al. 2000) and by better intellectual performances than DS individuals; these different profiles may lead to different ability to modulate the systems involved in maintaining posture which is greater in PWS with respect to DS individuals.

We demonstrated in previous studies (Cimolin, Galli, Vismara, et al. 2011) that both PWS and DS patients are characterised by unchanged postural stability when eyes are open and closed, showing that their balance is not influenced by visual input. The authors hypothesised that proprioception is prevalent over visual input in postural control in DS and PWS. Such abnormal modulations of the systems involved in balance maintenance are confirmed by the result obtained using the FD approach.

An important finding of this study is related to the effect of obesity on postural control. We observed, in fact, that the presence of differences between pathological groups (PWS and DS group) and OCG in terms of all analysed parameters leads to the consideration that overweight, which is one of the distinctive features in both PWS and DS, does not directly influence the postural maintenance in these two pathological states.

Our analysis showed that both PWS and DS patients yield a particularly impaired balance capacity, with DS individuals affected more than the PWS group. It is important to underline that this consideration is not clearly evident by the traditional parameters obtained with the time-domain approach but it is shown in particular by the frequency-domain and fractal method, which better explained the postural strategy in the two pathological states.

These results are important from a clinical point of view, as quantitative characterisation of postural strategy in PWS and DS may serve as a basis to develop, differentiate and enhance the rehabilitative options, indicating that DS individuals need a more intensive rehabilitative programme in comparison with PWS individuals. In particular, as we previously demonstrated (Galli et al. 2008; Cimolin, Galli, Vismara, et al. 2011) that balance is not influenced by visual input and that proprioception may be prevalent over visual input in the development and setting of postural control system in DS and PWS, the rehabilitative programme should also consider somatosensory exercises, particularly in DS patients, in addition to improving hypotonia, muscle strength, weight loss and motor control by proprioceptive training.

Based on our results, the frequency domain and FD approach seems to add relevant information to the time-domain analysis of the CoP. These analyses, considering the non-stationary nature of CoP signal, showed peculiarities in posture maintenance which were not

evident solely from the traditional ones. However, it is not a completely clear FD result in terms of postural control, particularly from a clinical point of view. The FD values may be interpreted as an inability to synergically modulate the three systems (i.e. visual, vestibular and somatosensory) involved in maintaining posture. The human body is continuously exposed to external perturbations, which we try to counteract by integrating the real-time inputs and the prediction system based on previous inputs. On the other hand, a more complex stabilometric pattern could be also interpreted as a characteristic of a successful vigilant strategy to keep balance. Both interpretations can be correct but the question is then how to decide which one is the most appropriate one in a case at hand and the debate is still open. More work is needed to identify the correct physiological interpretation of this parameter in a given condition. In addition, it is important to underline that an effort should be made to try the computational method; while at the moment time-domain and frequency-domain parameters are easily obtained using the user-friendly software for postural data analysis generally present in clinical settings, the computation of FD parameter is not yet obtained as it needs specific competencies.

The strength of this study could be twofold: first, the obtained results demonstrated that noteworthy information from a clinical point of view can be obtained using postural analysis, which is a user-friendly assessment using just a force platform, without specific subjects needing to prepare, and without requiring them to retain their underclothes. Secondly, the comparative analysis was carried out not only with normal weight but also with obese individuals, in order to highlight the role of weight and its influence on postural maintenance.

This study has some limitations. A low number of participants enrolled, particularly PWS, which resulted in limited strength of the clinical and statistical findings; it should however be reminded that PWS is a rare condition and that therefore enrolment of those patients is difficult. In addition, although we tried to acquire more than one trial the results presented in this study refer to only one trial, due to the subject's intrinsic factors at the moment of the trial acquisitions; a stricter analysis should be conducted considering more than one trial. Another bias is that participants were not compared in terms of orthopaedic characteristic, degree of muscle hypotonia and weakness and ligament laxity, and also cognitive impairment had not been measured nor compared between groups.

Declaration of interest
The authors do not have any conflicts of interest or financial interest. All authors attest and affirm that the material within has not been and will not be submitted for publication elsewhere.

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