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Gait strategy in patients with Ehlers-Danlos syndrome hypermobility type and Down syndrome

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ABSTRACT

People suffering from Ehlers-Danlos syndrome (EDS) hypermobility type present a severe ligament laxity that results in difficulties in muscle force transmission. The same condition is present in people suffering from Down syndrome (DS) even if their clumsy movements are due to cerebral and cognitive impairments. The aim of this study was to quantify the gait patterns of subjects with EDS and with DS using Gait Analysis (GA). We quantified the gait strategy in 12 EDS individuals and in 16 participants with DS. Both pathological groups were compared to 20 age-matched healthy controls in terms of kinematics and kinetics. Results showed that DS individuals are characterized by a more compromised gait pattern than EDS participants, even if both groups are characterized by joint hypermobility. All the patients showed significant decreased of ankle stiffness probably due to congenital hypotonia and ligament laxity, while different values of hip stiffness. These findings help to elucidate the complex biomechanical changes due to joint hypermobility and may have a major role in the multidimensional evaluation and tailored management of these patients.

1. Introduction

Ehlers-Danlos syndrome (EDS) is a relatively common rheumatologic condition which comprises a clinically variable and genetically heterogeneous group of inherited connective tissue disorders, mainly featuring joint hypermobility, skin hyperextensibility and tissue fragility (Callewaert, Malfait, Loeys, & De Paepe 2008). The various forms of EDS are characterized by abnormalities in the chemical structure of the body's connective tissues (for example, skin, muscles, tendons and ligaments) (Voermans et al., 2009). EDS results in weakness and/or excessive flexibility of the connective tissues of the body: as a result, skin may become fragile and joints unstable. People suffering from EDS type III present a severe ligament laxity that results in difficulties in muscle force transmission, showing muscle hypotonia, and in movement instability.

Recently, Galli et al. (2011) pointed out the typical features of gait pattern in a population with EDS: a non-physiological gait was observed by the authors. In particular, moreover the spatio-temporal parameters, all the differences between physiological and non-physiological gait pattern could be summarized in pathological kinematic and kinetic of the ankle joint, in terms of sustained plantarflexion and lower value of absorbed and generated work. They also investigated ankle and

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hip stiffness: the results evidenced a stiffness reduction in both joints compared to Control Group. As reported in the literature (Carr, 1970; Ferrell et al., 2004), the key feature of EDS gait is characterized by hypermobility that results in a decrease of joint stiffness and in the lack of a correct force transmission, and consequently in muscle hypotonia: these features, as well documented in literature (Dowdy-Sanders, & Wenger, 2006; Dyer, Gunn, Rauh, & Bery, 1990; Galli, Rigoldi, Brunner, Virji-Babul, & Albertini, 2008; Morris, Vaughan, & Vaccaro, 1990; Vieregge, Schulze-Rava, & Wessel, 1996; Weeks, Chua, & Elliott, 2000), are similar to the ones that afflict the movements of Down syndrome (DS) people.

Motor disability is widespread among individuals with DS. It includes longer motion and reaction times, balance and postural deficits, and cocontraction of agonist and antagonist muscles (Aruin, Almeida, & Latash, 1996; Shumway-Cook & Woollacott, 1985). The motor dysfunction in individuals with DS involves impaired muscle control, which is frequently referred to as "clumsiness" by parents and health professionals (Latash & Corcos, 1991) and Carr (1970) referred that the delay in motor development in DS is linked to the generalized muscle hypotonia and ligament laxity that is characteristic of the condition. Galli et al. (2008) documented the gait characteristics of children with DS and quantified the hip and ankle joint stiffness that characterize the gait pattern in individuals with DS: in their work pathological subjects pointed out higher values of hip joint stiffness as compensatory strategies in order to lower the numbers of degrees of freedom, and lower ankle joint stiffness as consequence of joint laxity and muscle hypotonia, which cause functional weakness.

As the common feature that characterized EDS and DS syndrome, ligament laxity and muscle hypotonia, aim of this work is to study the relationship between these and the gait pattern alterations in EDS and DS adult patients in order to characterize from a motor point of view the two syndrome.

2. Materials and methods

2.1. Participants

The gait pattern was investigated in a group of 12 participants (EDSG: Ehlers-Danlos Syndrome Group) with a diagnosis of EDS type III (mean age: 43.08 years, sd 6.78; range: 36–59 years) and in a group of 16 participants (DSG: Down Syndrome Group) with Down syndrome (mean age: 35.60 years, sd 4.43; range: 31–45 years): data were collected in the Posture and Motion Analysis Lab of IRCCS "San Raffaele-Pisana", TOSINVEST Sanità, Rome, Italy. All participants gave their informed consent to participate in the study and all investigations were performed in conformity with the ethical and humane principles of research. The researchers explained the purpose, procedures, risks, and benefits of the study to parents who gave their informed consent.

A group of 20 healthy adults was included as controls (CG: Control Group) (ten male and ten female; mean age: 37.23 years; sd 8.91; range 30–50 years): exclusion criteria for the CG included prior history of cardiovascular, neurological or musculoskeletal disorders. They showed normal flexibility and muscle strength and no obvious gait abnormalities.

2.2. Instrumentation and data acquisition

The equipment utilized for data acquisition during the gait trials consisted of a 12-camera optoelectronic system (ELITE2002, BTS, Milan, Italy) with a sampling rate of 100 Hz, two force platforms (Kistler, CH) with a sampling rate of 500 Hz and 2 TV camera Video system (BTS, Italy) synchronized with the system and the platforms for videorecording.

To evaluate the kinematics of each body segment, passive markers were positioned on the participants' body, as described by Davis, Ounpuu, Tyburski, and Gage (1991).

After placement of the markers, subjects were asked to walk barefoot at their own natural pace (self-selected speed) along a walkway (6 m) containing the force platforms at the mid-point. Three acquisitions comprehensive of kinematic and kinetic data were collected for each participant in order to guarantee data reproducibility: once the consistency was verified, the kinematic and kinetic data of one trial for each patient was considered for the analysis.

2.3. Data analysis

Starting from the markers coordinates, using a specific software, the kinematics of the lower limb joints during gait (i.e. pelvis, hip, knee and ankle 3D movements) were computed and represented as % of gait cycle. From the data recorded by force platforms, also the kinetic of hip, knee and ankle was analysed. From the graph representing these variables, some punctual indexes were computed.

In particular, concerning the spatio-temporal parameters, we computed the % stance (%ST), that is the percentage of stance phase of gait cycle; the mean velocity (MV), that is the mean velocity during the gait cycle, normalised to the individual's height (1/s); the anterior step length (ASL), normalised to individual's height.

Considering the kinematics, we calculated the mean value (MPT index) of pelvis tilt on sagittal plane and the mean value of foot progression (MFP) during the gait cycle; the values of the angle of ankle (AIC index), knee (KIC index) and hip joint (HIC index) at the Initial Contact (IC); the values of maximum of the hip flexion (HM index) during the gait cycle, the value of the maximum of the ankle dorsiflexion during stance phase (AMSt index) and the maximum of the flexion of the knee (KMSw index) during swing phase; the value of the minimum of ankle dorsiflexion in stance phase (AmSt index), the value of the minimum of the knee flexion in stance phase (KmSt index), and the value of the minimum of the hip flexion (HmSt index) in

stance phase; the range of motion, that is the difference between the maximum and the minimum value assumed by the joints, of the pelvis tilt (PS-ROM index) plane; the range of motion of the hip flexion–extension (HFE-ROM) plane; the range of motion of the knee flexion–extension (KFE-ROM index); the range of motion of the ankle dorsi-plantarflexion during gait cycle (ADP-ROM index).

About the kinetics during gait trial we computed the generated hip work (HGP index, J/kg) as the integral of the positive values of the hip power during stance phase; the absorbed hip work (HAP index, J/kg) as the integral of the negative values of the hip power during stance phase; the generated ankle work (AGP index, J/kg) as the integral of the positive values of the ankle power during stance phase; the absorbed ankle work (AAP index, J/kg) as the integral of the negative values of the ankle power during stance phase.

In order to evaluate the effect of ligament laxity and hypotonia on joint kinetics and kinematics, hip and ankle stiffness (hip stiffness: Kh index; ankle stiffness: Ka index) were expressed by plotting the values of the flexion–extension moment versus the flexion–extension angle over the gait cycle interval between 10% and 30%. The 10–30% interval (corresponding to the second rocker) of the gait cycle was selected and the linear regression was fitted. The angular coefficient of the linear regression corresponded to the joint stiffness index (Nm/kg degrees), as described in previous studies (Davis & De Luca, 1996; Frigo, Crenna, & Jensen, 1996). Knee stiffness was not included in this study due to the lack of linear relation between kinematics and kinetics.

For each participant (both patients and controls), three out of five trials, consistent in terms of gait pattern (spatio-temporal, kinematic and kinetic) were considered for analysis.

2.4. Statistical analysis

All the previously defined parameters were computed for each participant and then the mean values and standard deviations of all indexes were calculated for each group. Data of all the participants were compared using one-way ANOVA and LSD post hoc test, to detect the differences in the gait strategies between all the three groups considered. Null hypotheses were rejected when probabilities were below 0.05.

3. Results

In Table 1 we reported the clinical characteristics of the three groups compared in this work. Age and weight were not statistically different as height was: for this reason stride length was normalized to subject's height.

Concerning the gait parameters an initial comparison between left and right side was performed: no differences were found between the two limbs, so the data were pooled.

In Table 2 we reported the mean values and the standard deviation (in brackets) of spatio-temporal and kinematics parameters computed for all the groups considered. As concern spatio-temporal parameters EDS group evidenced higher values of gait velocity in comparison with DS group and comparable values in comparison with CG. The step length and the percentage of stance phase during gait cycle were significantly different from CG for both pathological groups even if EDSG pointed out closer values than DS did.

As concerning kinematic data, the MPT displayed statistical differences between pathological groups, evidencing higher values in DS participants than in EDSG, closed to normative data, and pointing out a more anteriorly flexed pelvis during gait. Also observing hip joint only the DS participants showed higher values of the HM index during swing and decreased value of the HmSt index in comparison with CG and EDSG. The analysis of knee joint indexes revealed statistical differences between DSG and all the other participants: DSG evidenced lower values of the KMSw and of KFE-ROM during gait cycle, instead of EDSG that reported values closed to normal data. Focusing on ankle joint, the analysis revealed statistical differences between the gait of EDSG and DSG: for quite all the indexes considered the two pathological groups pointed out statistical differences. The maximum plantarflexion (AmSt) at the end of stance phase and the ADP-ROM during gait cycle showed higher values for EDSG than for DSG and comparable values between EDSG and CG: EDS participants conserved the proper movement of the ankle in sagittal plane in order to guarantee the gait progression even of the presence of ligament laxity. The MFP evidenced an extrarotation for DS subjects, revealing a not-oriented movement in sagittal plane.

In Table 3 kinetic and stiffness indexes are reported for all the participants. Hip generated work (HGP, Fig. 1) showed comparable values between EDSG and CG but higher values for DS group. Concerning ankle generated work (AGP, Fig. 1), DSG and EDSG evidenced lower value than CG at statistical level, confirming the reduced ability to generate propulsion power.

Table 1
Clinical characteristics of the study groups. Data are expressed as mean (standard deviation).

Clinical characteristics	EDSG	DSG	CG
Age (years)	43.08 (6.77)	35.6 (4.43)	40.1 (4.8)
Weight (kg)	64.33 (16.76)	68.07 (12.13)	66.9 (8.5)
Height (cm)	162.83 (4.80)[*,+]	152.2 (7.5)[§]	173.3 (5.01)

[*] $p < 0.05$, EDSG versus DSG.
[+] $p < 0.05$, EDSG versus Control Group.
[§] $p < 0.05$, DSG versus Control Group.

Table 2
Spatio-temporal and kinematic parameters of the study groups. Data are expressed as mean (standard deviation).

	EDSG	DSG	CG
Spatio-temporal parameters			
%ST	59.7 (4.65)	63.1 (3.75)	59.65 (3.19)
MV (1/s)	0.89 (0.32)*	0.68 (0.17)§	1.12 (0.18)
ASL	386.8 (134.7)+	406.8 (103.3)§	0.88 (0.21)
Kinematics indexes (degrees)			
Pelvis			
MPT	8.6 (5.14)*	17.54 (7.2)§	6.53 (6.97)
PS-ROM	6.8 (3.95)	4.11 (2.95)	3.62 (0.86)
Hip			
HIC	29.46 (9.15)	35.21 (11.84)	27.23 (9.57)
HFE-ROM	41.55 (5.82)	39.53 (8.88)	43.52 (4.76)
HmSt	−9.5 (8.09)*	−2.33 (6.36)§	−14.83 (9.6)
HM	30.91 (7.2)*	38.93 (10.36)§	33.45 (6.89)
Knee			
KIC	5.96 (7.34)*	11 (7.57)§	4.39 (6.53)
KMSw	58.32 (7.5)*	42.71 (16.1)§	57.08 (6.63)
KmSt	−0.3 (6.71)	1.4 (6.45)	0.12 (3.82)
KFE-ROM	56.84 (6.03)*	41.3 (12.49)§	59.07 (6.31)
Ankle			
AIC	−4.10 (5.48)	−0.12 (7.94)	1.81 (6.87)
AMSt	10.66 (4.16)*,+	14.05 (5.93)§	21.04 (5.16)
AmSt	−14.29 (6.7)*	−1.82 (4.91)§	−9.73 (9.40)
ADP-ROM	22.75 (4.26)*	10.08 (6.82)§	25.72 (6.56)

* $p < 0.05$, EDSG versus DSG.
\+ $p < 0.05$, EDSG versus Control Group.
§ $p < 0.05$, DSG versus Control Group.

Table 3
Kinetics parameters of the study groups. Data are expressed as mean (standard deviation).

	EDSG	DSG	CG
Kinetics (J/kg)			
HGP	9.44 (4.79)*	17.86 (10.84)§	11.08 (7.32)
HAP	5.6 (4.23)+	2.22 (2.75)§	12.6 (9.18)
AGP	21.61 (8.01)*	14.41 (6.9)§	30.72 (8.75)
AAP	7.45 (2.93)	8.72 (4.33)	9.77 (5)
Joint stiffness (Nm/kg degree)			
Kh	0.015 (0.006)+	0.016 (0.006)§	0.02 (0.007)
Ka	0.056 (0.03)+	0.067 (0.02)§	0.083 (0.03)

* $p < 0.05$, EDSG versus DSG.
\+ $p < 0.05$, EDSG versus Control Group.
§ $p < 0.05$, DSG versus Control Group.

Observing the joint stiffness results, the analysis revealed that EDSG and DSG were significantly different in terms of hip stiffness (Kh): while EDSG showed mean values lower than CG as consequence of ligament laxity, DSG evidenced a significantly stiffer hip as compared to EDSG and CG. As for ankle stiffness (Ka), no statistical differences appeared between EDSG and DSG: both pathological groups were characterized by reduced values in comparison with CG.

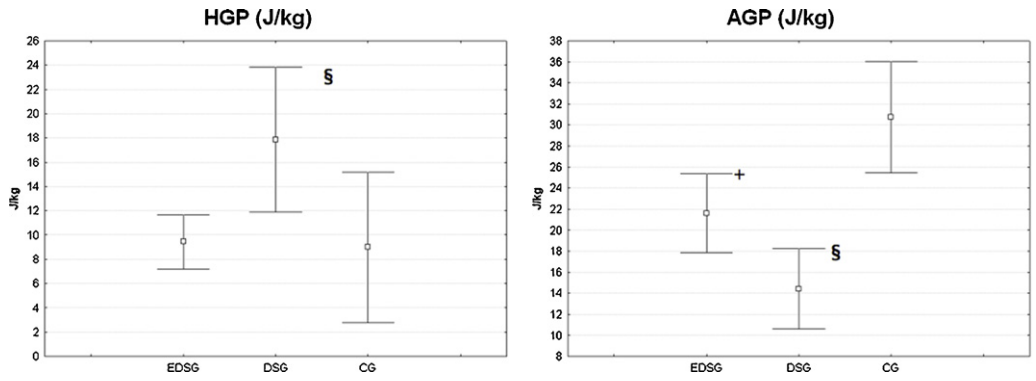

Fig. 1. Hip and ankle generated power for both pathological groups and for controls. *$p < 0.05$ EDSG versus DSG. +$p < 0.05$, EDSG versus Control Group. §$p < 0.05$, DSG versus Control Group.

4. Discussion and conclusion

Joint hypermobility is the common feature between Down syndrome and Ehlers-Danlos syndrome: this hypermobility is due to the ligament laxity that characterized both the syndromes. The hypermobility not only determines passive hyperextension of the joints but also has important biomechanical consequences on gait pattern: this consideration emphasizes the importance of a careful and precise evaluation of EDS and DS syndrome, yielding crucial information in establishing the level of disability and in identifying the correct therapeutical program considering not only the results of the ligament laxity but also investigating the kinematic and the kinetics of all the involved joint and their compensatory strategies.

Both the investigated pathological groups revealed non-physiological gait patterns but while statistical differences between DSG and healthy subjects were evident in quite all the analysed indexes at every considered levels, the statistical differences between EDSG and healthy subjects are concentrated in few of them and, in particular, at ankle joint. Focusing on spatio-temporal parameters, these indexes pointed out statistical differences between EDSG and DSG in terms of MV, %ST and ASL, evidencing lower values of these indexes for DS participants: these parameters indicate a cautions gait pattern, mainly focused in maintaining equilibrium rather than in guaranteeing gait progression.

Considering kinematic data focusing on hip, DSG reported a lower value of HmSt respect to CG and EDSG: the sustained flexed position of the hip during the gait cycle is in according to the higher value of pelvic tilt for DS participants and it is probably linked to the needing, from one hand, of lowering the COM (centre of mass) in order to better control the equilibrium and, from the other hand, of shifting the COM in an anterior position in order to facilitate the compromise progression force. As for knee joint, DSG were characterized by lower value of the KFE-ROM, due to the reduction of KMSw, evidencing a reduced mobility of the joint: this strategy probably enforces the values reported for the hip joint. The reduction of KFE-ROM reflects a minor use of this joint: aiming at balance and stability, DSG probably tend to reduce the degrees of freedom to control during gait. The ankle joint concentrated more differences between pathological groups than the other joints did: for all the computed indexes, in terms of kinematic, EDSG evidenced values very close to healthy subjects, except for the value of the AMSt, but statistical different from the indexes computed for DSG. The analysis revealed lower value of the AmSt in terminal stance and a reduced ADP-ROM for DS participants. Moreover, DSG exhibited an accentuated MFP for all the gait cycle. DSG were characterized by a poor propulsion force and the position of the foot indicates a dispersion of this force, and consequently an ankle generated power reduction as reported in the following, in a medio-lateral component, used as compensatory strategies aiming at balance.

Hip kinetic data evidenced an increased HGP for DS participants in comparison with EDSG, which demonstrated values closed to healthy subjects. As for ankle kinetics, both pathological groups pointed out lower value of AGP, more pronounced for DS participants: the ligament laxity and the muscle hypotonia play an important role in the gait progression.

Concerning Kh and Ka, EDSG pointed out lower values in comparison with CG in both ankle and hip joint confirming the presence of ligament laxity. As for DS participants while the Ka is comparable with the one computed for EDSG, the Kh is higher in comparison with EDSG and CG: this is probably linked to the needing of blocking the joint in order to diminish the degrees of freedom during gait.

Basing on the literature and the typical feature between Ehlers-Danlos syndrome and Down syndrome, both pathological groups started from the same condition regarding ligament laxity and consequently joint hypermobility, but they assumed different compensatory strategies to overcome their lack, probably due to the fact that EDSG presents no neurological disorders, as DSG did, and they have to overcome the disability due only to the ligament laxity. While EDSG conserved the multilink configuration of the kinematic chain, maintaining all the freedom degrees as healthy subjects did, DS participants tried to compensate their precarious equilibrium feeling downing the centre of mass, flexing the knee and excluding this joint from the kinematic chain, reducing its movements, as documented by the ROM reduction at knee level and by the increased absorbed work at hip level. In order to guarantee the gait progression DSG shifted the movements from distal to proximal joints that permitted them to improve the postural control during gait.

Moreover, one typical feature of DSG gait pattern was the shifting of the main gait plane from sagittal to frontal: as reported in the results, the extrarotation of the foot progression (MFP) for DSG revealed an involving of frontal plane during gait and so force propulsion dispersion in terms of generated work useful in sagittal progression, as documented also by the AGP reduction.

From these considerations, considering them from a clinical point of view, the quantitative characterization of gait patterns in EDSG and DSG is important to identify, develop and enhance the rehabilitative options, and the comparison between two pathologies that present the same ligament laxity condition would help the therapists in knowing deeply how and where the rehabilitation program would be concentrated: EDSG probably need a muscle power program in order to increase the force transfer instead of DSG that, before the muscle power program, would probably relearn the correct scheme of gait.

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