Accepted: 25 May 2017

DOI: 10.1111/hae.13297

ORIGINAL ARTICLE

Musculoskeletal

WILEY Haemophilia

Sensory strategies of postural sway during quiet stance in patients with haemophilic arthropathy

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Introduction: The sensory strategies of postural control in adult haemophilic arthropathy patients are still poorly understood.

Aim: To determine sensorial posture-control strategies through postural sway frequency analysis when in a bipedal quiet stance with and without visual stimulus deprivation in healthy subjects and patients with haemophilic arthropathy. Secondarily, to determine the irregularity of postural balance control through sample entropy (SampEn).

Methods: A triaxial accelerometer attached at the L3 level determined the displacement and acceleration of the centre of mass (DCoM and ACoM, respectively) under open- and closed-eyes conditions. Sensorial strategies were studied by spectral analysis of the DCoM signal, divided into low, medium and high frequencies for visual/vestibular, cerebellum and somatosensory strategies respectively. DCoM irregularity was also analysed by SampEn.

Results: Fifteen young, healthy subjects and fifteen young, haemophilia patients were included. The mediolateal DCoM and anteroposterior ACoM differed between groups. During the open-eyes condition, haemophiliacs presented limited high and medium frequencies, and more low frequency bands as compared to non-haemophiliacs ($P<.05$). In the closed-eyes condition, haemophiliacs had a minor percentage of high frequencies but an elevated percentage of low frequencies as compared to non-haemophiliacs ($P<.05$). Non-haemophiliacs had higher SampEn than haemophiliacs in the mediolateral axis with open- and closed-eyes ($P<.05$ and $<.001$, respectively).

Conclusions: The presented results indicate that patients with haemophilic arthropathy, as compared to healthy subjects, have less postural control irregularity and poor somatosensory system contributions that are compensated by more vestibular inputs.

KEYWORDS

centre of mass, haemophilia, haemophilic arthropathy, postural control, sample entropy, somatosensory

1 | INTRODUCTION

Haemophilic arthropathy is one of the most expensive and disabling complications for patients with haemophilia.[1] This multifactorial, complex process damages joints through an inflammatory response in synovial joints, which, in turn, occurs as a consequence of repeated haemarthrosis phenomena.[2,3] Muscle function and proprioception are directly affected by joint damage,[4] and haemophilic patients further exhibit a connection between the degree of joint damage and proprioceptive impairment.[5] Proprioception is defined as a spatial sense of limb/body position and movement.[6] Receptors found in the muscles, joints, ligaments and skin transmit proprioception to regulate total posture (ie postural equilibrium) and segmental posture (ie joint stability).[7] Closely related to proprioception is postural control, which is the spatial control of body position for balance and orientation.[8] Importantly, impaired proprioception might affect postural control, resulting in increased risks of falling, functional deterioration and suffering new or recurrent injuries. Therefore, postural control assessments, which involve proprioception, are relevant aspects considered when screening functionality in patients with haemophilia.[9,10]

Postural control is a complex interaction between the sensory and motor systems.[11] To achieve control, different sensory strategies must be generated for environmental adaptation responses to occur. These strategies are classified as visual/vestibular, cerebellum and somatosensory, as per task requirements and the most predominate system involved in task execution.[11,12] The contributions of these systems to postural control have been assessed by spectral analysis during sway balance, with low, medium and high frequencies divided into correspondence to visual/vestibular, cerebellum and somatosensory strategies respectively.[13-16] Low frequency energy, visual/vestibular strategies are highest in healthy subjects during bipedal postural control when deprived of visual inputs, as compared with an open-eyed condition.[13] Furthermore, the degree of motor skills developed through subject experiences (eg sports level, ie power law of practice) influences the sensory strategies involved in task execution.[16]

Automaticity and attention when in a quiet stance have been studied under different conditions and during motor-learning process via regularity analyses for postural sway.[17-19] This is a relevant aspect for motor task development and for establishing the minimum conscious effort needed to perform a balance task. The automaticity of postural control can be assessed through sample entropy (SampEn), which determines the complexity or regularity of a signal within a time-series data set. A high SampEn expresses greater signal irregularity and could be interpreted as more automaticity and less attention given to a task, such as holding a quiet stance.[17-20] Furthermore, patients with joint hypermobility (ie Ehlers-Danlos syndrome) have less irregularity and more displacement for centre of pressure in comparison to normal laxity subjects.[21] In contrast, subjects with greater athletic skill (eg gymnasts) have more irregularity and more stable postural control,[19] suggesting that while these subjects have a greater ability to maintain optimal posture, they require less cognitive resources.

Postural control is usually tested by centre of pressure analysis using force plates. Centre of pressure is related to motor outputs from the ankle joint. However, multijoint postural models also relate the proximal/distal joints (ie hip and ankle) to postural control contributions, with consequent implications in controlling the centre of mass (CoM).[22,23] Assessing the CoM is useful for evaluating postural control during quiet standing when comparing young, elderly or post-stroke patients.[24,25] Therefore, the CoM could be an alternative force-platform measure for analysing developmental changes in upright postural control.[24]

Triaxial accelerometry of the trunk has been used to estimate acceleration of the CoM (ACoM) to ultimately assess balance control in an upright stance.[26-28] Accelerometers present various advantages, including being compact (ie hand-held), inexpensive compared with force platforms and easy to use in diverse postural control assessment conditions, such as in clinical contexts.[26-28] Accelerometer signals also are effective in detecting changes between different conditions, such as age groups,[19,26-28] and represent a potential clinical tool for assessing sensorial postural control strategies and the automatic control of postural balance.

Despite existing tools and a relevant need, only some aspects of static postural control are known for adult and paediatric haemophilia patients, as compared with healthy people.[9,10,29] Currently, only one case report proposes that haemophilic arthropathy may affect performance during sensorimotor stability tasks and subsequent learning[30]; however, more studies are needed to corroborate this assumption. To deeply understand postural control in individuals with haemophilia, and thus contribute towards improved balance-training programmes, research must be conducted on the sensorial postural control strategies needed in bipedal tasks and on the irregularity of postural balance.

Therefore, the main aim of the present study was to apply postural sway frequency analysis to determine the sensorial postural control strategies used by patients with haemophilic arthropathy and young healthy subjects when in a bipedal quiet stance, with and without visual stimuli. A secondary aim was to determine the irregularity of postural control. We hypothesized that patients with haemophilic arthropathy would have less postural control; irregularity in the displacement of the CoM (DCoM); less high frequency energy, somatosensory system contributions; and major low frequency energy, vestibular/visual input contributions as compared to young healthy subjects.

2 | MATERIALS AND METHODS

Ethical approval was obtained from the Northern Metropolitan Health Service of Santiago, Chile, and written informed consent was obtained from each participant.

2.1 | Patients

All haemophilia patients were evaluated according to Gilbert[31] and the Haemophilia Joint Health Score (HJHS) v2.1.[32] Haemophilia patients were excluded if they had a history of lower limb surgery, intra-articular or muscular bleeding in the lower or upper limbs within the

TABLE 1 Basal anthropometric characteristics of control and haemophilia groups

	NHG	HG	*P*-values
Age (years)	21.9 (1.4)	21.8 (3.9)	.570
Body weight (kg)	69.7 (9.0)	65.4 (10.7)	.390
Height (m)	1.70 (0.1)	1.72 (0.1)	.905
BMI (kg/m^2)	23.6 (2.5)	22.0 (2.2)	.172

Data are expressed as the mean (standard deviation).
BMI, body mass index; HG, haemophilia group; NHG, non-haemophilia group.

TABLE 2 Haemophilia Joint Health and Gilbert scores

	Ankle		Knee			
	Right	Left	Right	Left	Global gait	Total points
HJHS	4.0 (0-14)	4.4 (0-15)	3.2 (0-9)	3.5 (0-15)	1 (0-4)	15.1 (0-33)
Gilbert	1.5 (0-6)	2.3 (0-6)	2.1 (0-6)	1.9 (0-7)	N.A.	7.9 (0-16)

Haemophilia Joint Health Score (HJHS): Total score range, 0-20 points for ankle or knee; global gait, 0-4 points; total points are expressed as the sum of scores for the knees and ankles. Gilbert score: total score range, 0-12 points for ankle or knee; total points are expressed as the sum of scores for the knees and ankles. Data are expressed at the mean (min-max).
N.A., not applicable.

last 3 months, an ankle sprain or inhibitors. Intra-articular or muscular bleeding of the upper limbs, considered as pain, is a potential factor that could affect postural control.[11] Non-haemophilia subjects were excluded if they had any acute injury of the lower limbs within the last 3 months, a history of surgery or any rheumatologic disease.

Fifteen young haemophilia patients and fifteen young healthy subjects were recruited. The basal anthropometric characteristics of the sample groups are presented in Table 1. All patients presented severe haemophilia A. The joints assessment by the Gilbert and HJHS are described in Table 2. In both joints, only one patient scored zero points.

2.2 | Data acquisition

A triaxial accelerometer (ENGtotal Ltda., Santiago, Chile) with a 3 g range and 0.001 g sensitivity detection[27] was used. The accelerometer was attached at the level of the L3 lumbar spinous process[28] of each participant using a Velcro™ belt (3M, St. Paul, MN, USA). Anteroposterior, mediolateral and axial signals were recorded at a 250 Hz sample frequency. Then, the acceleration signals were filtered using a fourth-order Butterworth lowpass filter with a 6 Hz cut-off frequency.[13]

2.3 | Balance assessments

All subjects were assessed while barefoot and were instructed to stand quietly in a bipedal posture for 30 s. Subjects were tested with their eyes opened and closed. Each condition was tested three times, with 2 min of rest between tests. A visual marker was placed at eye level 1 m away from the participant.[28] All tests were conducted between 9:00 AM and 11:00 AM[33,34]

2.4 | Data analysis

All signals were analysed by the Matlab 2015 software (Mathworks Inc., Natick, MA, USA). For ACoM, the root mean square was used. The triaxial accelerometer obtained DCoM signals following the method previously established by Mayagoitia et al.[27] Then, the root mean square was applied to DCoM.

To calculate the frequency bands, a fast Fourier transform of the data was performed to determine the spectral energy of each frequency band, expressed as a percentage of the total spectral energy. The frequency bands of DCoM aligned with previous definitions in the literature.[13,16] Specifically, the low frequency band (0-0.5 Hz) corresponded to the pronominal actions of the visual and vestibular systems; the medium frequency band (0.5-2 Hz) corresponded to the pronominal regulation of the cerebellum; and the high frequency band (>2 Hz) corresponded to the pronominal control of the somatosensory system. The SampEn of the resulting DCoM position was calculated using a Matlab® routine from PhysioNet,[35] with input parameters according to Lakhani et al.[18] The length of sequences to be compared (*m*) was equal to 3, and the pattern similarity tolerance (*r*) was equal to .04 (Figure 1).

2.5 | Statistical analysis

Sample size was calculated in accordance with a previous report on posturographic analysis of balance control in patients with haemophilic arthropathy.[10] Considering an accepted alpha risk of .05 and beta risk of .01 in a one-sided test, 15 haemophilic and 15 non-haemophilic subjects were needed to establish differences of ≥.07 cm as statistically significant in the mediolateral axis during the open-eyes condition. The common standard deviation was assumed to be .042 cm, and a 20% drop-out rate was anticipated.

Descriptive data from the current study were expressed as the mean (and standard deviation). An alpha error <.05 was used to establish significance. Data distribution was determined by a Shapiro-Wilk's test. Excluding mediolateral ACoM and anteroposterior DCoM data during the open-eyes condition, all data were normally distributed and analysed through parametric tests. The excluded data were assessed through non-parametric tests to describe the mean and range of data.

For comparisons between groups, the non-parametric samples were analysed by the Mann-Whitney *U* test, while independent samples were evaluated with the parametric Student's *t* test. For comparisons between open- and closed-eyes conditions, the *t* test and Wilcoxon tests were used. Lineal regression was applied to determine the relationships between postural control strategies, DCoM, and SampEn. All statistical analyses were performed using the statistical program IMB SPSS Statistics v20 (IBM Corp, Armonk, NY, USA).

3 | RESULTS

Detailed results for ACoM and DCoM group comparisons are shown in Table 3. In haemophiliacs under both visual conditions, ACoM values were greater ($P<.05$) in the anteroposterior axis and DCoM

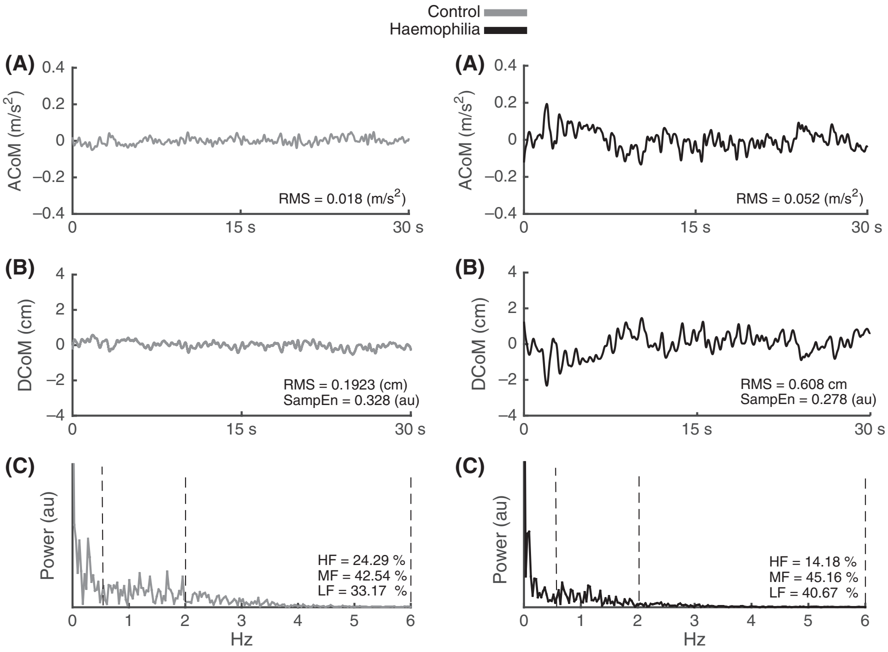

FIGURE 1 Postural behaviour in the mediolateral axis of two subjects during the open-eyes condition. Left: non-haemophilia, control subject (grey). Right: haemophilia patient (black) with a Gilbert score of 15 points (ie summed points for the knees and ankles). (A) Comparisons for the acceleration of the centre of mass (ACoM). (B) Comparisons for the displacement of centre of mass (DCoM). (C) Frequency energy analyses for the DCoM per band, including high frequency (HF), medium frequency (MF) and low frequency (LF) energies. Au, adimensional unites; RMS, root mean square; SampEn, sample entropy.

values were greater (*P*<.05) in the mediolateral axis, as compared to healthy subjects. For comparisons between visual conditions, non-haemophiliacs showed increased ACoM values (*P*<.05) in the mediolateral axis and increased DCoM values (*P*<.05) in the anteroposterior axis during the closed-eyes condition (Table 3).

Regarding frequency comparisons between groups, only the mediolateral axis showed significant differences between groups. During the open-eyes condition, haemophiliacs presented a minor contribution of high and medium frequencies (*P*<.05) and a greater contribution of low frequency bands as compared to non-haemophiliacs. In the closed-eyes condition, haemophiliacs had a minor percentage of high frequencies but a high percentage of low frequencies as compared to non-haemophiliacs (*P*<.05; Figure 2).

For spectral energy band comparisons between conditions, the closed-eyes condition induced a significant decrease (*P*=.001) of high frequency energy (19.55% [2.20]-17.03% [2.04]) but a significant increase (*P*=.005) of low frequency energy (49.04% [5.50]-52.60% [4.25]) in the anteroposterior axis of non-haemophiliacs. In turn, haemophiliacs only showed a significant decrease of high frequency energy (17.19% [3.29]-15.55% [3.89]) when in the closed-eyes condition in the mediolateral axis.

In the results related to SampEn analysis, non-haemophiliacs showed a higher SampEn than haemophiliacs in the mediolateral axis under both the open- and closed-eyes conditions (*P*<.05 and *P*<.001, respectively). However, in the anteroposterior axis, haemophiliacs had a higher SampEn (*P*<.05; Table 4). Regarding SampEn comparisons between conditions, non-statistical differences were found (Table 4).

For the relationship between postural control strategies in the mediolateral axis, the incorporation of both groups in the linear regression analysis showed a negative relationship between irregularity and DCoM (*P*<.001) in both the open- and closed-eyes conditions. Both conditions also exhibited a positive relationship between irregularity and high frequency energy (*P*<.001; Figure 3).

4 | DISCUSSION

The primary aim of this study was to determine the sensorial postural control strategies of haemophilic arthropathy patients, as compared to non-haemophiliacs, through spectral energy analysis of postural sway when in a bipedal stance, with and without visual stimuli. A secondary aim was to determine the irregularity of postural balance. The obtained results support the proposed hypothesis that haemophilic arthropathy patients, as compared to healthy subjects, have less postural control irregularity and less somatosensory system contributions that are compensated with more vestibular input contributions.

Regarding postural control assessments by DCoM, haemophiliacs had poorer CoM control in the mediolateral axis (ie worse control in the coronal plane) than non-haemophiliacs under both visual conditions. This finding could be an expression of lesser hips and trunk control[8,22]; however, haemophilia patients showed greater joint damage in the knees and ankles.[2] Furthermore, this result could be a manifestation of deficient multijoint coordination between the trunk and lower limbs for optimizing postural control.[23,36] Moreover, the ACoM in the anteroposterior axis was higher in haemophiliacs in both the open- and closed-eyes conditions, suggesting a diminished capacity of the ankle to maintain the CoM stable.[8]

Considering CoM irregularity, the obtained results support a negative relationship between SampEn and DCoM. This would be in line with previous reports in which less postural control translated into less irregular sway balance.[19,21] Furthermore, the decreased SampEn of haemophiliacs in the mediolateral axis could be associated with less automaticity or more attention during postural control.[19,20] These

TABLE 3 ACoM and DCoM in control and haemophilia groups

Condition	*Axis*-signal	NHG	HG	*P*-values
OE	*AP*-ACoM (m/s^2)	.02 (.01)	.04 (.02)	.002*
	ML-ACoM (m/s^2)	.05 [.03-.08]**	.05 [.03-.12]	.868
	AP-DCoM (cm)	.55 [.30-.86]**	.54 [.31-1.28]	.709
	ML-DCoM (cm)	.22 (.09)	.43 (.20)	.001*
CE	*AP*-ACoM (m/s^2)	.02 (.01)	.05 (.03)	.012*
	ML-ACoM (m/s^2)	.07 (.02)**	.06 (.02)	.493
	AP-DCoM (cm)	.73 (.24)**	.67 (.24)	.472
	ML-DCoM (cm)	.25 (.09)	.52 (.36)	.013*

Normally distributed data distributed are expressed as the mean (standard deviation). Non-normally distributed data are expressed as the median [min-max].

ACoM, acceleration of the centre of mass; AP, anteroposterior axis; CE, closed-eyes condition; DCoM, displacement of centre of mass; HG, haemophilia group; ML, mediolateral axis; NHG, non-haemophilia group; OE, open-eyes condition.

*Statistical significance *P*<.05 between control and haemophilia groups.

**Statistical significance *P*<.05 between open- and closed-eyes conditions.

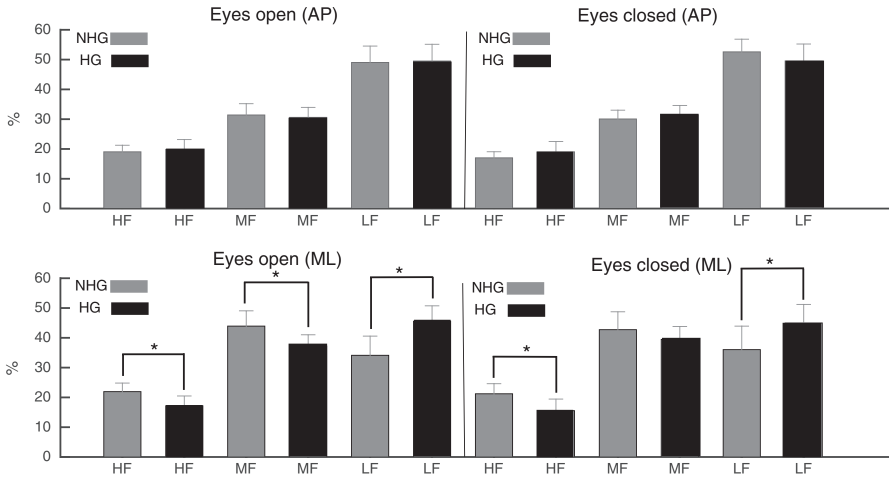

FIGURE 2 Energy frequency analyses for the displacement of centre of mass in control, non-haemophilia (NHG) and haemophilia (HG) groups during the open- and closed-eyes conditions in the anteroposterior (AP) and mediolateral (ML) axes. HF, high frequency energy; MF, medium frequency energy; LF, low frequency energy. Statistical significances between NHG and HG indicated by *P<.05.

TABLE 4 SampEn for centre of mass displacement in the control and haemophilia groups

Condition	*Axis*-SampEn	NHG	HG	*P*-values
OE	*AP*-SampEn	.21 (.05)	.22 (.06)	.607
	ML-SampEn	.31 (.03)	.22 (.05)	<.001**
CE	*AP*-SampEn	.18 (.04)	.22 (.05)	.039*
	ML-SampEn	.30 (.04)	.24 (.05)	.001*

AP, anteroposterior axis; CE, closed-eyes condition; HG, haemophilia group; ML, mediolateral axis; NHG, non-haemophilia group; OE, open-eyes condition; SampEn, sample entropy.

Normally distributed data are expressed as the mean (standard deviation).

*Statistical significance *P*<.05 between control and haemophilia groups.

**Statistical significance *P*<.001 between control and haemophilia groups.

overall findings suggest that tasks involving CoM stability require more conscious effort for haemophilia patients than non-haemophiliacs.

Additionally, a positive relationship was found between SampEn and high frequency energy (somatosensory system), while a negative relationship existed between SampEn and low frequency energy (vestibular system). The less irregularity of postural sway in joint dysfunctions (ie haemophilia arthropathy) could be an expression of a minor contribution to somatosensory postural control feedback, with increased attention in the visual/vestibular feedback systems.[21] The recorded lesser contribution of the somatosensory system and greater contribution of vestibular/visual inputs in haemophiliacs, as compared to non-haemophiliacs, is in line with the sensory weighting theory, which suggests that the postural control system changes sensory input weights to optimize stance.[8]

The sensorial strategies employed by haemophilia patients when in a quiet stance are poorly understood, but the present research provides integral insight into this subject. The applied methodology could be used to determine the progress of balance rehabilitation,[18,37] to establish which sensorial strategies are better suited for physical therapy programmes (eg visual-somatosensory feedback or only improve the somatic planter),[30,38] to ascertain the effects of automaticity in postural control,[18] and to improve postural control interventions so as to prevent intra-articular reinjuries in patients with haemophilia.

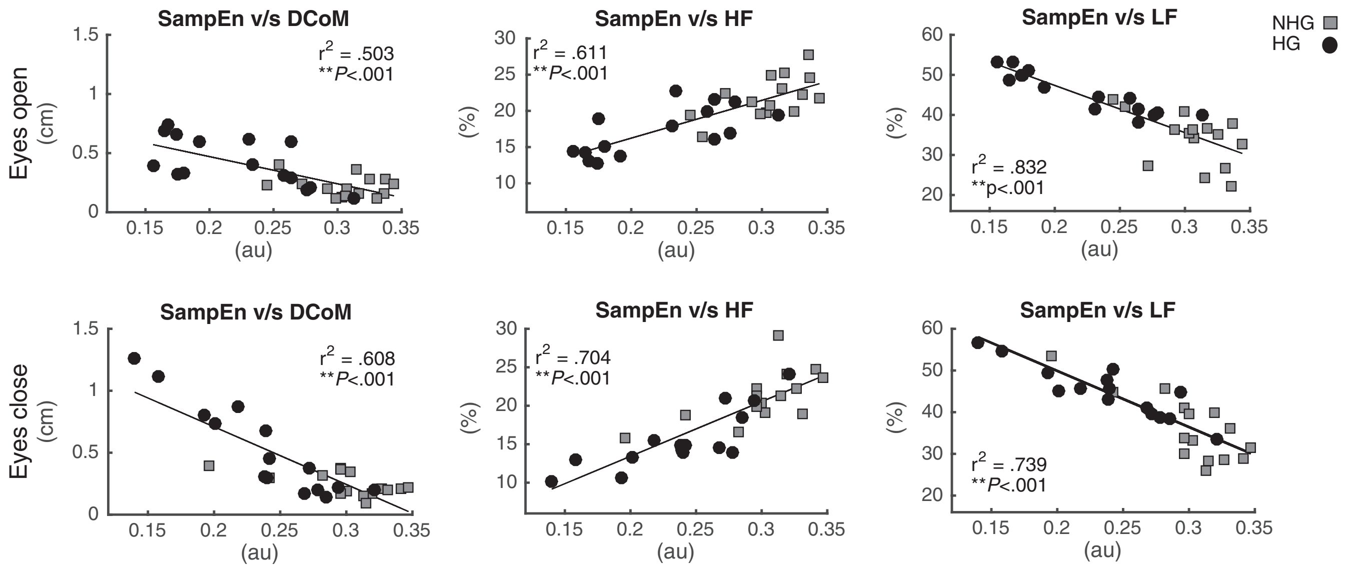

FIGURE 3 Lineal regressions for the mediolateral axis of the non-haemophilia (NHG) and haemophilia (HG) groups during the open- and closed-eyes conditions. Left: sample entropy (SampEn) vs displacement of the centre of mass (DCoM). Middle: SampEn vs high frequency (HF) energy analyses for DCoM, corresponding to the somatosensory system. Right: SampEn vs low frequency (LF) energy analyses for DCoM, corresponding to the vestibular system. Au, adimensional units. Statistical significances indicated by **$P<.001$.

Previous studies have used energy band frequency analyses to determine sensorimotor strategies when in a quiet stance for patients with Down syndrome,[13] anterior cruciate ligament reconstruction of knee,[39] stroke,[40] neuropathic conditions[37] and dyslexia,[15] as well as in the context of sports.[14] However, to the best of our knowledge, this is the first report to confirm that joint deterioration in haemophilia patients is accompanied by different sensorial strategies for postural control, as compared to non-haemophilia subjects. The obtained band frequency results in non-haemophiliacs are in accordance with previous studies.[13,16] Namely, healthy subjects increase low frequency energy (ie visual/vestibular) for static postural control when without visual stimuli.[13] This compensatory strategy was not found in haemophiliacs. Furthermore, the results of the current study support previous reports on static balance in adult and paediatric haemophilia patients, who present poorer motor control than non-haemophilia subjects.[9,10,29]

Regarding the applied methodology, accelerometers are a cheap, useful and easily portable alternative for postural control assessments in clinical practice,[26-28] especially for undeveloped and developing countries. Indeed, the ACoM may be a low-cost alternative to force platform measurements for assessing static postural control in clinical and research contexts,[24] such as already demonstrated by the Nintendo Wii Balance Board®.[29]

The current study presents several limitations worth mentioning. Only CoM behaviour was analysed, but future research might consider measuring both CoM and centre of pressure considering multijoint models of postural control.[22,23] Together, these measurements could improve on and corroborate the present results. In addition to this, an integral approach with surface electromyography in the lower limbs and trunk could help elucidate the motor strategies used by haemophiliacs during postural tasks.[36] Furthermore, radiological exams such as computed tomography, magnetic resonance imaging and sonography were not used in the current assessments. These radiological data would help to determine the relationship between joint damage and sensory control strategies. As such, future studies should used more demanding tasks, such as the unipedal balance stance, to compare haemophiliac patients with and without arthropathy, particularly as a bipedal quiet stance could be insufficient for discriminating haemophiliac patients with and without joint arthropathy.[10] Overall, further research is needed to more fully understand the implications of pain in postural control and attention during balance tasks.[11]

Regarding assessments of postural control irregularity, future studies with more complex tasks (eg dual tasks) are needed to corroborate automaticity and attention during balance exercises in patients with haemophilic arthropathy.[8] Finally, future reports need to consider different age ranges as results in children might be applicable in preventing arthropathy and results in older people might help prevent falls.

5 | CONCLUSION

The presented results indicate that patients with haemophilic arthropathy, as compared to healthy subjects, have less postural control irregularity and poor somatosensory system contributions compensated by more vestibular inputs. The applied methodological approach could be useful for analysing the sensory strategies of postural control when in a quiet stance and for determining the motor control progress of a postural exercise programme in patients with haemophilia.

ACKNOWLEDGEMENTS

The authors thank the Haemophilia and Inherited Bleeding Disorder Treatment Centre of the Roberto del Río Hospital, and particularly Estefania Figueroa and Nicole Pavez, for facilitating the recruitment of haemophilia patients.

DISCLOSURES

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

AUTHOR CONTRIBUTION

CCM performed the research, designed the research study, contributed essential reagents or tools, analysed the data and wrote the paper. CDLF designed the research study, contributed essential reagents or tools, analysed the data and wrote the paper. GRL contributed essential reagents or tools, analysed the data and wrote the paper. SMC performed the research, contributed essential reagents or tools, analysed the data and wrote the paper. VS analysed the data and wrote the paper. FQ analysed the data and wrote the paper. SPA designed the research study, contributed essential reagents or tools, analysed the data and wrote the paper.

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How to cite this article: Cruz-Montecinos C, De la Fuente C, Rivera-Lillo G, et al. Sensory strategies of postural sway during quiet stance in patients with haemophilic arthropathy. *Haemophilia*. 2017;23:e419–e426. https://doi.org/10.1111/hae.13297