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#### ABSTRACT

This article describes a conglomerate measure of gait variability based on nine spatiotemporal parameters: the Gait Variability Index (GVI). Concurrent validity, inter-session reliability and minimum detectable change (MDC) were evaluated in 31 patients with Friedreich's Ataxia (FRDA), through comparisons with classically used evaluation tools such as the International Cooperative Ataxia Rating Scale (ICARS).

GVI scores for the healthy population were 100.3  $\pm$  8.6 and were significantly reduced in FRDA patients (70.4  $\pm$  7.9). The GVI was correlated with the global ICARS score and was sensitive enough to differentiate between groups of FRDA patients categorized by the Posture and Gait Disturbances sub-score. The GVI was found to have a high inter-session reliability with an intraclass correlation coefficient of 0.91. A MDC of 8.6 points was found necessary to ensure that a change in GVI reflects a true change rather than measurement error.

The GVI provides a quantitative measure of variability which behaves well statistically in both HP and patients with FRDA. It can be easily implemented using the supplemental data provided with this article. Complementary work is necessary to strengthen the GVI validation.

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## 1. Introduction

Balance control during gait can be affected by different pathologies which alter stability (capacity to recover from perturbations), thus leading to falls. Because this is an important public health issue, many studies have attempted to identify markers relating to fall risk.

Gait analysis techniques provide objective data including spatiotemporal parameters (STP). Two approaches have been used

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0966-6362/\$ - see front matter © 2013 Elsevier B.V. All rights reserved. http://dx.doi.org/10.1016/j.gaitpost.2013.01.013 to assess fall risk from STP. The most classical approach is based on comparison of mean values between healthy subjects and patients; it has caused a paradox which has been well described. The same characteristics are associated with an increased risk of falls and have also been explained as the adoption of a safer, more stable gait strategy [1]. The second approach is based on the measure of reproducibility of coordinated limb movements from one step or one stride to the next. This within-trial variability could be assessed using an analysis of the fluctuation magnitude (the variance, the size of fluctuations) [2]. There are indications that fall risk can be more precisely evaluated by the STP variability rather than by mean values [2,3]. Although gait variability was originally considered to represent noise, more recent research suggests that it reflects the underlying motor control and may be relevant to quantify age-related and pathological alterations in locomotor control-system, as well as to provide a clinical measure of mobility and functional status [2]. Subtle changes in variability have been reported among identified older fallers [4] and in future fallers [3]. Variability has also been reported to increase under dual-task conditions, when walking on irregular surfaces or with the eyes

<sup>\*</sup> Clinical trial registration: Data are parts of the following clinical trial: NCT00811681 (http://clinicaltrials.gov/).

Abbreviations: CV, coefficient of variation; FAPS, Functional Ambulation Performance Score; FRDA, Friedreich's Ataxia; GDI, Gait Deviation Index; GVI, Gait Variability Index; HP, healthy population; ICARS, International Cooperative Ataxia Rating Scale; ICC, intraclass correlation coefficient; MDC, minimum detectable change; PCA, principal component analysis; PGD, ICARS "Posture and Gait Disturbances" sub-score; STP, spatiotemporal parameters.

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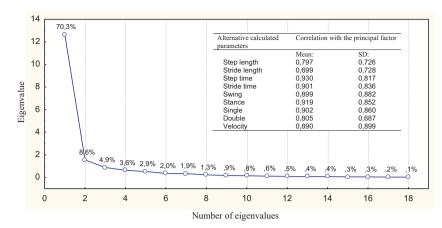


Fig. 1. Results for PCA: Eigenvalues, explained variance, and correlation coefficient c<sub>n</sub> of each parameter with the main identified factor (Eigenvalue 1, 70.3%).

closed [5–7]. Recently, gait variability has been used as a primary outcome measure in randomised controlled trials [8,9].

However, a recent review of the clinimetric properties of gait variability [10] highlighted the lack of consensus regarding the methods used to analyse variability. Some questions remain unresolved regarding its use in clinical settings. There is also a lack of consensus regarding which STP should be selected. We found 11 STP for which variability has been calculated, although step length and stride time are most frequently analysed [3,10]. Some studies used SD, while others used the coefficient of variation (CV). Another question is the meaningfulness of the amount of variability; is only high variability meaningful or should low variability also be taken into account? Excessive or reduced step width variability has been associated with falls in older persons [3,11]. Low step width variability could indicate a lack of compensation for instability [12], however it could simply be a consequence of the greater stride width, frequent in fallers [3]. As for other gait data, the interpretation of interdependent parameters remains complex and requires clinical expertise. The use of a conglomerate index such as for kinematic and kinetic data (Gillette Gait Index, Gait Deviation Index (GDI), GDI-Kinetic [13–15]) reduces this problem by accounting for interdependence. The Functional Ambulation Performance Score (FAPS) can be used to evaluate the functional aspects of gait [16]. To our knowledge, there are no indices to quantify gait variability based on STP.

Our purpose was threefold: (1) to develop an index of gait variability based on STP: the Gait Variability Index (GVI), (2) to explore concurrent validity in patients with Friedreich's Ataxia (FRDA) through comparisons with classically used evaluation tools, and (3) to evaluate the magnitude of change necessary to ensure that changes reflect true changes, i.e. the minimum detectable change (MDC) [17]. FRDA is a neurodegenerative disease in which there is a combination of cerebellar, pyramidal syndromes and axonal neuropathy causing coordination deficits, loss of proprioception and balance difficulties, in static conditions and during gait. The rapid degenerative nature causes instability and falls with increasing frequency over short periods. In this context, the GVI could be used to more precisely quantify gait variability, to monitor progress over time or to gauge the effects of a therapeutic intervention.

## 2. Methods

The principal aim was to define a metric distance in order to quantify the proximity between parameters which could reflect gait variability in a patient and the same parameters in a healthy population (HP). Formalization of GVI was carried out in three phases: (1) selection of pertinent parameters, (2) assignation of weightings relating to the natural degree of variance, (3) calculation of the distance between patients and HP.

#### 2.1. Raw/alternative parameters

9 STP were chosen to compute GVI: step length (cm), stride length (cm), step time (s), stride time (s), swing time (s), stance time (s), single support time (s), double support time (s), velocity (cm/s). Each parameter has been used at least once in the literature to quantify gait instability or fall risk using the SD or CV [3,10]. However, these measures of dispersion present a bias which could alter the index or limit its use: SD is sensitive to the scale, CV tends to infinity when the mean is close to 0. An alternative solution was found and calculations were carried out to create 18 new parameters for each leg. We differentiate between limbs because left/right variability can be different when the level of deficit and/or the control capacity differs between limbs [18,19].

For gait at comfortable velocity, the values for a given parameter are divided so that the left and right legs are considered separately. The first operation consists of separating the values obtained in different trials and expressing each as percentage of the mean of the series to which it belongs (e.g. left leg, first trial). If one value is equal to the mean of the series, it is given a value of 100. The aim is to reduce the influence of inter-trial variability when several trials are necessary or when patient's gait is not at all reliable from one trial to another, therefore, it is the intra-trial variability which is being assessed. By calculating the SD of each series (SD is not problematic because all data are based on 100) and taking the average for each leg, it would have been possible to obtain a measure of variability of each parameter. However, this could be influenced by pace changes (e.g. resulting from constant acceleration during the test or from fatigue) inducing larger SD. Therefore, the absolute differences between consecutive values from a same series are calculated instead. Lastly, mean and SD of all absolute differences are calculated, yielding two values for an initial raw STP: the mean evaluates the fluctuation magnitude and the SD provides an additional measure of the fluctuations consistency. This procedure is repeated for the nine raw STP, giving 18 alternative parameters  $(p_n)$  for each lower limb.

#### 2.2. Weighting

Data from 250 subjects (aged 12–65), patients with varied pathologies and healthy subjects, were included to determine the weight of each parameter. Previous studies have indicated that STP variability changes after the age of 7 due to the gait maturation. Adult-like values occur from the age of 11–12 years [16,20].

The only inclusion criterion was independent gait, using no technical/human assistance. STP were recorded during bare-foot gait at comfortable velocity on GAITRite<sup>TM</sup> mat (v4.0<sup>1</sup>) with 2 m run-up and 2 m exit, without counting the inactive mat areas. Recordings were carried out in two centres with different lengths of mats (488, 610 or 732 cm). A minimum of three trials were recorded to obtain a minimum of five absolute differences for the calculation of the 18 parameters for each leg ( $250 \times 2 \times 18$  parameters).

Principle component analysis (PCA) is classically used to reduce large quantities of information into a smaller number of components [13]. In this study, PCA was used to determine the relationship between the individual parameters and the global gait variability. We hypothesized that one principle component related to "variability" would explain a large amount of variance of the data, which was indeed the case. One principle factor alone explained 70.3% of variance. The parameters were all correlated with this axis and the coefficients of correlation were between 0.687 and 0.930 (Fig. 1). These coefficients were kept for use as weights in the GVI calculation.

<sup>1</sup> Suppliers: CIR Systems Inc., 8 John Walsh Blvd, Peekskill, NY 10566, USA.

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## 2.3. GVI

The HP consisted of 123 subjects (aged 12–62) and was used to calculate the normal values of GVI ( $123 \times 2 \times 18$  parameters). Recording conditions were identical to those described previously.

For an individual  $\alpha$ , the 18 parameters  $p_n$  are multiplied by their respective correlation coefficient  $c_n$ , then the sum of the products is calculated thus:

$$s^{\alpha} = \sum_{1}^{18} (p_n \cdot c_n) \tag{1}$$

The next part of the calculation and the interpretation are similar to the GDI [14]. It is important that the result of a clinical test can be read quickly and interpreted easily. We believe that the final form of GDI completely fulfils this pre-requisite.

 $s^{\text{HP}}$  represents the mean sum in the healthy population. The distance  $d^{\alpha,\text{HP}}$  between the parameters of a subject  $\alpha$  and those of the HP is:

$$d^{\alpha,\mathrm{HP}} = \left\| s^{\alpha} - s^{\mathrm{HP}} \right\| \tag{2}$$

A raw index is obtained by the formula:

$$GVI_{raw}^{\alpha} = \ln \left( d^{\alpha, HP} \right) \tag{3}$$

Next, the z-score is calculated, i.e. the number of SD separating the raw score of a subject  $\alpha$  from the raw score of the HP:

$$zGVI_{raw}^{\alpha} = \frac{GVI_{\alpha}^{raw} - Mean (GVI_{HP}^{raw})}{SD(GVI_{HP}^{raw})}$$
(4)

Finally, the *z*-score is multiplied by 10 and subtracted from 100:

$$GVI^{\alpha} = 100 - 10 \times zGVI^{\alpha}_{raw}$$
<sup>(5)</sup>

It is possible to obtain a mean GVI from the left and right indexes.

By definition, the mean score and SD of the reference population are respectively 100 and 10. A GVI  $\geq$  100 indicates that the patient has a similar level of variability as the HP (neither too little nor too much). Each 10 point difference corresponds to a separation of one SD from the HP score, indicating that the variability of the subject is greater than or less than the amount of variability found in normal gait.

#### 2.4. Pathological population

31 patients (aged 12–25) with FRDA were included to validate the score in a population with dynamic instability. These patients were followed for 2 years at 6 monthly intervals. At each assessment, the same tests were carried out: STP recorded on the GAITRite<sup>TM</sup> with calculation of FAPS and mean GVI; timed 8 m-walk; manual muscle strength of the lower limbs [21]; the International Cooperative Ataxia Rating Scale (ICARS), which evaluates the principle elements of the cerebellar syndrome, a higher score indicates greater disability [22]. ICARS is multidimensional and includes items which not only evaluate posture and gait but also kinetic function of the upper and lower limbs, verbal and oculomotor dysfunctions. We chose to compare GVI with the "Posture and Gait Disturbances" sub-score (PGD) to be more precise.

During the first assessment, each patient carried out a second gait recording session, 2 days after the first to evaluate the inter-session reliability. Only data from trials of unassisted gait were used, the data from 81 assessments. Some patients contributed several sets of data (respectively 6, 9, 2 and 7 patients carried out 1, 2, 3 and 4 assessments). All data were, however, analysed as independent samples.

#### 2.5. Statistics

In order to explore the concurrent validity of GVI in FRDA patients, it was compared with the GVI of the HP using *t*-test. Pearson's correlations were used to investigate relationships between GVI, ICARS and clinical results in the patient group. An alpha-level of 0.05 was considered as significant.

To assess the behavior of GVI with regard to the degree of balance and gait impairment, patients were categorized into three sub-groups according to their PGD score. ANOVA and post hoc tests (Fisher's LSD) were carried out to identify differences between sub-groups.

Inter-session reliability for FRDA patients was reported as an intra-class correlation coefficient (ICC) of type (3,1) and interpreted according to Shrout and Fleiss [23]. An ICC > 0.75 indicates excellent, 0.75–0.40 moderate to good and <0.40 poor reliability. Then, SE and MDC were calculated to quantify the magnitude of change necessary to ensure a real change in GVI.

### 3. Results

In healthy subjects (Table 1 and Fig. 2a), the mean GVI was 100.3  $\pm$  7.6. This is slightly different to 100  $\pm$  10 since we studied the mean GVI. In comparison, GVI of FRDA patients (70.4  $\pm$  7.9, Fig. 2b) were significantly lower (p < 0.01). It must be noted that all GVI were

### Table 1

GVI for HP and FRDA subjects and categorization by "Posture and Gait Disturbances" ICARS subscale score.

Subjects	Ν	Mean (SD)	Range	Normal distribution
Healthy	123	100.3 (7.6)	83-124	Yes
FRDA	81	70.4 (7.9)	51-90	Yes
[1-9]	17	75.6 (6.1)	68-89	Yes
[10-17]	48	71.3 (6.9)	57-90	Yes
[18-25]	16	61.9 (5.4)	51-74	Yes

normally distributed according to the Shapiro–Wilk test. The mean, SD and range of the other tests are given in Table 2 as well as the correlation of each with GVI in FRDA population. Clinical worsening of symptoms was reflected by increase in global ICARS score, PGD subscore and time required to walk 8 m and by decrease in FAPS and muscle strength. The GVI was found to correlate significantly with all tests, particularly with the PGD sub-score ( $r^2 = 0.46$ ) but little with muscle strength ( $r^2 = 0.06$ ).

The PGD scores were normally distributed from 1 to 25 in FRDA group (Table 1). Patients were categorized into three sub-groups of impairment (Fig. 2c–e): PGD scores between 1 and 9 (N = 17), between 10 and 17 (N = 48) and between 18 and 25 (N = 16). Patients with higher and lower PGD scores had respectively lower and higher GVI. Fisher's LSD test identified significant differences (p < 0.05) between all groups.

The inter-session reliability for GVI in FRDA patients was high (Table 3), with ICC of 0.91 and confidence interval of 95% from 0.82–0.96. SE and MDC at 95% were respectively 3.1 and 8.6 points.

## 4. Discussion

The GVI was developed for objective quantification of gait variability. The parameters chosen had to be obtainable in patients with limited walking distance or who required technical aid, as well as in less affected patients. The STP fit this criterion and although a GAITRite<sup>TM</sup> was used in this study, they can be calculated in many ways. The results showed that GVI behaved well statistically in both HP and patient groups. It can easily be implemented using the supplemental data provided with this article.

Balance problems arise in FRDA as soon as the first clinical symptoms occur. We considered that it was appropriate to evaluate GVI in this population and to compare it to standard clinical tests. Consistent with earlier studies in cerebellar ataxia [24,25], STP variability was higher in the FRDA group compared with the HP group and, de facto, GVI was lower in the patients. Our results showed that GVI was correlated with the ICARS but particularly with the PGD sub-score. The GVI also appeared to scale with the clinical assessment and to be sensitive enough to differentiate between the FRDA groups categorized by PGD sub-score.

A moderate correlation was found between GVI and FAPS and also the 8 m-timed walk. Indeed, it could be considered that these two tests evaluate dynamic balance but are more focused on the functional aspect of gait. If variability increases with lower walking speeds [24], it appears that ataxic patients spontaneously choose a speed which is close to the most stable gait, that is with the minimal possible variability for them [24]. In this way, changes in the average STP such as decreased velocity (which has repercussions on FAPS and 8 m-timed walk) do not necessarily cause an increase in variability. Reducing gait velocity can increase dynamic stability. We believe that it is important that both the functional and variability aspects should be assessed to give a more representative picture of gait.

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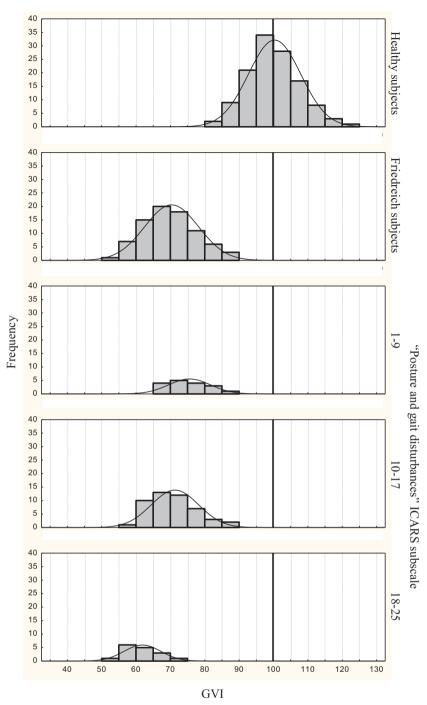


Fig. 2. Histograms of the GVI categorised by the "Posture and Gait Disturbances" ICARS sub-score. The normal distribution curve is shown for comparison, and the heavy vertical line indicates the mean values for the control group (GVI = 100).

The reliability of GVI was evaluated in the FRDA group. The GVI showed good inter-session reproducibility, better than that of the variability measures taken individually. Few studies have evaluated the reliability of SD or CV but there are some indications that

they are less reliable than the mean values;  $ICCs \leq 0.63$  were found in elderly subjects who carried out two 4 m timed walks [26].

For clinical tests, it is important to evaluate how much change is necessary in order to signify a true improvement/worsening. The

### Table 2

Means, standard deviations and ranges for the other clinical measures in FRDA subjects and Pearson's correlations with the GVI.

Measures	Mean (SD)	Range	Pearson's R	$R^2$	Threshold $p <$
FAPS (/100)	88.9 (11.9)	44-100	0.56	0.32	0.01
8 m walk test time (s)	6.0 (2.6)	3.7-18.7	-0.57	0.33	0.01
Lower limb testing (/50)	46.3 (3.4)	34-50	0.24	0.06	0.05
ICARS (/100)	29.8 (10.0)	5-56	-0.54	0.29	0.01
PGD subscale (/34)	13.3 (4.8)	1-25	-0.68	0.46	0.01

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Table 3

Intraclass correlation coefficient (ICC), standard error of measurement (SEM) and minimum detectable change (MDC) for D1-D2 FRDA's GVI (n=31).

Mean (SD)				ICC (3,1) (95% CI)	SEM	MDC
D1	D2	Difference	p (t-test)			
68.7 (9.6)	70.1 (10.8)	3.9 (2.4)	0.08	0.91 (0.82-0.96)	3.1	8.6

MDC suggests that a change of 9 points in GVI is necessary in FRDA patients.

The present study has limitations with regard to the number of strides used to compute the index. Owing and Grabiner found that accurate estimation of step kinematic variability required at least 400 steps while walking on a treadmill [27]. Hollman found that 60 strides were required to calculate variability in stride velocity during normal walking in elderly subjects [28]. In our work, each GVI was calculated from minimum of five absolute differences, which corresponds to 13 consecutive steps. Furthermore, the raw STP were obtained from several walks on GAITRite<sup>™</sup>. Paterson showed that STP variability differs depending if data are obtained from single, continuous trial or multiple short trials [29]. This was taken into consideration in the conception of GVI by trying to reduce inter-trial variability. We recommend the use of the highest number of cycles possible but, based on the recommendations of the European GAITRite<sup>TM</sup> Network Group about clinical evaluation of cycle-to-cycle variability [30], three values for each alternative parameter is the minimum requirement for GVI calculation. In our opinion, the most important consideration for use of GVI (or for measurement of gait variability) in the clinical assessment is to make sure that the conditions are always similar.

We proposed an index to improve the quantification of gait variability. The results obtained in FRDA patients seem to support the use of GVI. Future studies should continue to validate the measure; however, the GVI provides a useful method for many studies of variability and stability.

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## **Conflict of interest statement**

The authors of this manuscript have no financial or personal relationships with other people or organizations that could inappropriately bias this work.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.gaitpost.2013.01. 013.

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