Walking stride interval variability in patients with diabetic Charcot foot: A pilot study

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Abstract

Introduction: The variability of human walking has been studied for about twenty years. It appears not to be random but long-term autocorrelated, *i.e.* on time scales corresponding to several hundreds of gait cycles. It has been shown that the central nervous system (CNS) plays an important role in this variability. Indeed, people with CNS alterations have a different autocorrelation pattern than healthy individuals. In this pilot study, we address the question of the peripheral nervous system (PNS) influence on this long-term variability through the assessment of gait in patients with diabetic Charcot foot.

Methods: The population included 4 patients with diabetic Charcot foot and a control group of 6 healthy individuals. Ages were matched in both groups. Patients walked on a treadmill and the accelerations of their right ankle during the walk were recorded using a homemade inertial sensor. The acceleration versus time was used to calculate the durations of successive gait cycles. These stride intervals time series were analyzed by calculating several parameters related to variability: coefficient of variation (CV), Hurst exponent and sample entropy.

Results: Gait speed and average stride interval were significantly lower and higher in the Charcot group respectively. The coefficient of variation was significantly higher in the Charcot group. Hurst exponent and sample entropy were also greater in the Charcot group, though non significantly.

Conclusion: Patients with diabetic Charcot foot have a slower walk. Their long-term stride interval variability has a larger amplitude (larger CV) and predictibility (larger Hurst exponent) than healthy individuals. It is tempting to relate these features to an increased risk of fall.

Keywords: variability, charcot foot, walk, nonlinear analysis, orthopedic shoe.

1 Introduction

Human walking is a quasi-periodic phenomenon whose long-term variability, *i.e.* the fluctuations of a given parameter during time scales typically larger than 200 gait cycles, is not random. As shown by Haussdorff and collaborators (1995), long-term autocorrelations are observable in stride interval (SI) time series, that is the durations of successive gait cycles. The autocorrelations may be assessed by the

computation of indices such as Hurst exponent, related to the predictability of SI time series. The physiological origin of these long-term properties is yet to be clarified. Several mechanisms or systems may be involved. First, walking biomechanics may generate autocorrelations. Some mechanical inverted pendulum models of walk show indeed patterns typical of healthy walk (Gates, Su & Dingwell 2007). Second, the central nervous system (CNS) certainly plays a role. It is known that neurodegenerative conditions such as Parkinson's or Huntington's diseases alter the long-term structure of walking. We refer the interested reader to the meta-analysis of Moon *et al.* (2016), or to Lheureux *et al.* (2020) for recent results and references about Parkinson's disease. The role of peripheral nervous system (PNS) is poorly known. Gates & Dingwell (2007) have shown that diabetic peripheral neuropathy does not alter the variability of walk. In the latter study, peripheral sensory status was assessed by Semmes-Weinstein monofilaments at several locations on the bottom of the foot.

The purpose of this pilot study is to investigate further the role of PNS by studying the effect of diabetic Charcot foot on gait variability. Charcot foot is a rare complication of diabetic neuropathy. It leads to an acute foot inflammation and chronic joint or bone damage and ulcers. An orthopedic deformity (loss of mobility) is therefore added to the neuropathy (loss of sensitivity). Note that patients with Charcot foot use orthopedic shoes with a thick sole that normalize the pressure profile when patient's foot is put on the ground. The variability of the walk in patients with diabetic Charcot foot will be assessed by resorting to nonlinear analysis, in the spirit of the works by Crevecoeur, Bollens, Detrembleur & Lejeune (2010) and by Dierick, Nivard, White & Buisseret (2017).

2 Material & methods

2.1 Population

The Charcot group (Charcot) is made of 4 patients with radiologically confirmed unilateral Charcot foot deformity (left foot), at stage 3 (consolidation) on Eichenholtz scale (Rosenbaum & Di Preta 2015). They had no ulcer nor amputation. Patients were recruited from the diabetes department of the University Hospital Saint Luc in Brussels. They had to be able to walk without assistance on a treadmill, at spontaneous speed, with their own orthopedic shoes.

The control group (CTRL) is made of 6 healthy people whose data are taken from the free online database of Goldberger *et al.* (2002). Ages were chosen to match at best with the Charcot group, see Results.

2.2 Protocol

Patients from the Charcot group (men: n=3, women: n=1, duration of diabetes: 27 [21-29.5] years) walked on a treadmill for 15 minutes at a self-selected pace. A home-made inertial sensor named DYSKIMOT (Hage *et al.* 2019) was placed on the subject's right ankle just above the lateral malleolus. The three-dimensional acceleration and angular velocity time series were recorded at a sample frequency of 100 Hz. Patient's spontaneous walking speed was recorded on flat ground during a 10-meter walking test before walking on the treadmill. The same experimenter (S.C.) was in charge of the measurements. The protocol was approved by the ethics committee of the University Hospital Saint Luc. The identification number of the protocol is 'Charcot01'.

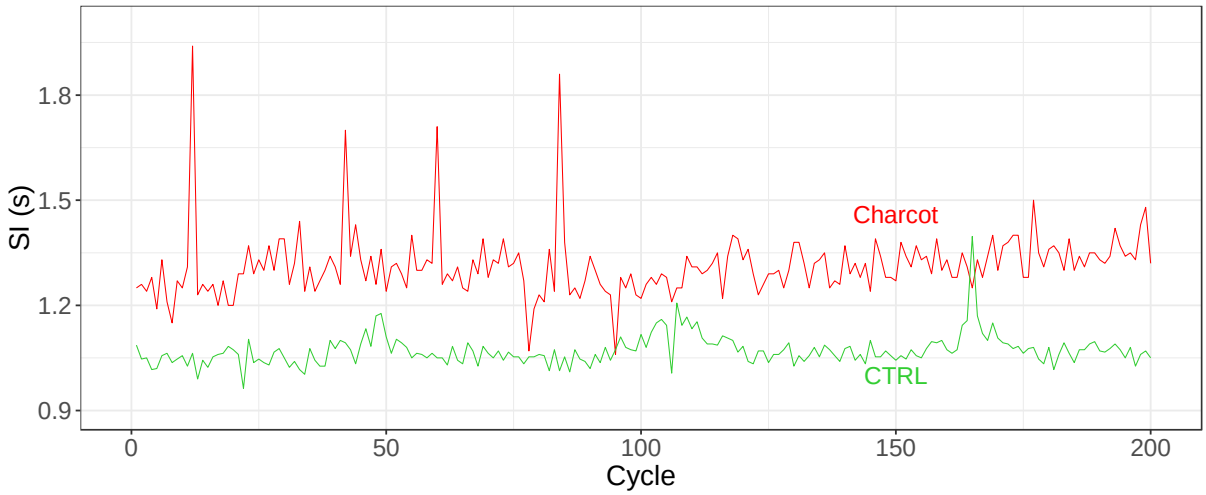

Figure 1: Typical traces of 200 consecutive stride intervals (SI) in a healthy participant (CTRL) and in a patient with Charcot foot (Charcot) walking on a treadmill.

2.3 Data analysis

The SI time series were computed by identifying the consecutive minima of the sagittal acceleration. All time series were truncated to a length of 256 points. Typical traces are displayed in Fig. 1. For each time series, the average SI, denoted T, was computed. Then, three variability indices were computed. First, the coefficient of variation, $\mathrm{CV} = \frac{\mathrm{SD}}{\mathrm{T}}$, with SD the SI standard deviation, quantifies the magnitude of SI variability. Second, the Hurst exponent, H RRA, assesses the predictibility of the SI time series. It was computed using the rescaled range analysis, which is more suitable for time series as short as 256 points (Warlop *et al.* 2017). A value of H RRA of around 0.5 denotes a random process, while values close to 1 denote a highly autocorrelated process. H RRA is typically between 0.5 and 1 for healthy individuals (Moon *et al.* 2016), this value being typical of chaotic systems. Third, the sample entropy, S, assesses the complexity of SI time series, or in other words, its amount of disorder. It is computed according to the method presented in the work by Yentes *et al.* (2013).

The parameters recorded in the two groups were compared by using a Mann-Whitney U test with significance level of 0.05. Treadmill and flat-ground speed in the Charcot group were compared by using a Wilcoxon signed-rank test with significance level of 0.05.

T, CV, H RRA and S were computed by using R free software. Statistical tests were performed by using Sigmaplot 11 (Systat Software, Inc.).

3 Results

Age and body-mass-index (BMI) were not significantly different between Charcot and CTRL groups: 57 [55-59] years *vs* 59 [53-67] years (p=0.769), and 28.9 [26.1-31.0] kg m^{-2} *vs* 22.5 [21.9-23] kg m^{-2} (p=0.097) respectively. Results are given under the form median [Q1-Q3].

Gait speed on the treadmill was significantly different between Charcot and CTRL groups: 1.5 [1.2-2.0] km h^{-1} *vs* 4.8 [4.6-5.4] km h^{-1} (p<0.01) respectively. Moreover, patients from the Charcot group walked significantly faster on flat ground than on the treadmill: 3.7 [3.3-3.9] km h^{-1} *vs* 1.5 [1.2-2.0] km h^{-1} (p=0.014) respectively.

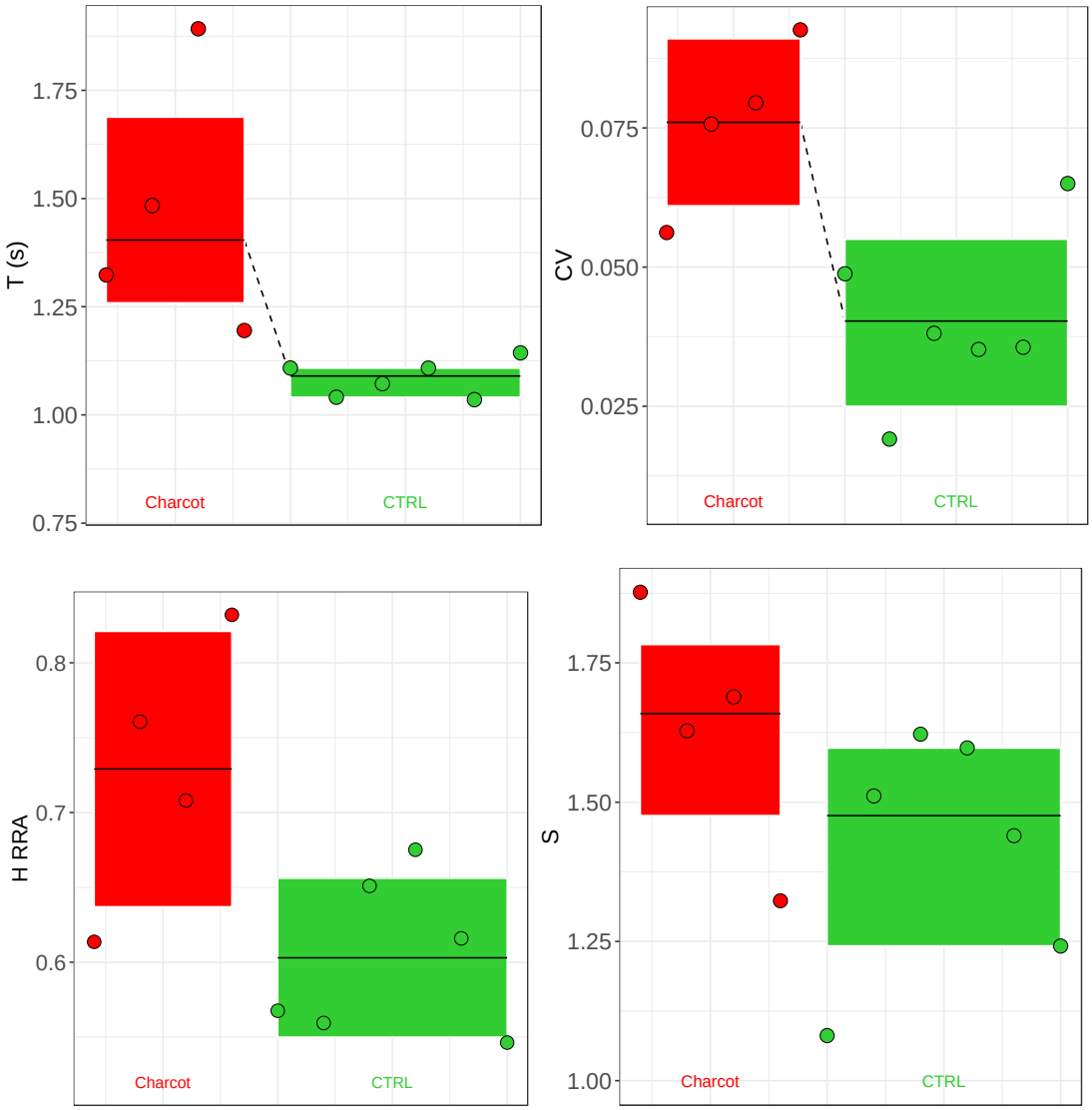

Figure 2: Individual results (points) and first and third quartiles (rectangles) for Charcot and CTRL groups. Significant differences between medians are marked by lines linking the medians.

Two parameters were significantly higher in the Charcot group: T with the median values of 1.40 [1.26-1.67] s *vs* 1.09 [1.04-1.11] s (p=0.004) respectively, and CV with the median values of 0.076 [0.061-0.091] *vs* 0.040 [0.025-0.055] (p=0.004) respectively.

The other two variability parameters were both higher in the Charcot group, although the differences were not significant: H RRA with the median values of 0.729 [0.637-0.821] *vs* 0.603 [0.550-0.656] (p=0.068) respectively, and S with the median values of 1.66 [1.48-1.78] *vs* 1.48 [1.24-1.60] (p=0.273) respectively. The results can be visualised in Fig. 2.

4 Discussion

Gates & Dingwell (2007) have made a first attempt to study the role of PNS in long-term gait variability. They compared diabetic patients with peripheral neuropathy to control subjects. They found a significantly lower walking speed for patients with peripheral neuropathy and no difference in Hurst exponent. Charcot foot being a complication of diabetes with orthopedic deformity, we expected that more important effects could be observed using a similar methodology.

A recent study in patients with Charcot foot at the same stage highlighted the slower walking speed and smaller steps to reduce pressure on the pathological foot (Motawea, El-Nahas & Armostrong 2019). We indeed observed that the Charcot group walked slower than the CTRL group on the treadmill. The fact that the Charcot patients were able to walk faster on the ground shows that the treadmill was perceived as uncomfortable for those patients; this treadmill-generated anxiety should be regarded as a limitation of our methodology. Future investigations on Charcot patients should favour studies on flat ground. We also found a larger T for the Charcot group, which is coherent with the reduced speed.

We now focus on variability indices. As recently discussed by Dierick *et al.* (2021) (see also the references therein), any deviation from healthy state should lead to a higher CV. In accordance with this finding, the Charcot group had significantly higher CV than the CTRL one. The origin may result in a poorer motor control due to altered proprioception caused by the neuropathy implied by the Charcot foot. Therefore, both PNS impairment may cause an increased CV in the case of Charcot foot.

The median value of H RRA was not significantly different between the CTRL and Charcot groups. The median value of H RRA in our CTRL group is smaller than the typical value of 0.75 found for young healthy individuals (Ravi *et al.* 2020). However, it has been shown that H RRA decreases with aging (Dierick *et al.* 2021). Interestingly, Charcot patients reach values of H RRA closer to young healthy individuals. We can speculate that it is an effect of their orthopedic shoes, although further studies are needed to check this assumption.

The sample entropy of patients in the Charcot group was higher than that of the CTRL group, even if this was not statistically significant. In other words, the distribution of SI durations was closer to a random process in the Charcot group. Such an increased sample entropy has also been found in patients suffering from Parkinson's disease (Coates *et al.* 2020).

This pilot study brings evidences that, despite wearing orthopedic shoes, patients with Charcot foot demonstrate an increased gait variability. If we consider the alteration of variability as a criterion of falling risk as proposed by Hausdorff, Rios & Edelberg (2001), it is then possible that patients with Charcot foot have a higher risk of falling than healthy subjects.

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