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USE OF NON-LINEAR METRICS FOR THE CHARACTERIZATION OF HUMAN MOTION: METHODOLOGICAL CONSTRAINTS AND FUNCTIONAL INTERPRETATION

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A me,
A chi l'ha reso possibile…

C'era una volta…
- Un re! - diranno subito i miei piccoli lettori.
No, ragazzi, avete sbagliato.
C'era una volta un pezzo di legno.

Carlo Collodi – Pinocchio

"We know that today, education is still the key to real and lasting freedom - it is still true today. So it is now up to us to cultivate that hunger for education in our own lives and in those around us. And we know that hunger is still out there - we know it."

Michelle Obama - Commencement speech at Dillard University
New Orleans, May 10 2014

Science means constantly walking a tightrope between blind faith and curiosity;
between expertise and creativity;
between bias and openness;
between experience and epiphany;
between ambition and passion;
and between arrogance and conviction,
in short, between an old today and a new tomorrow.

Heinrich Rohrer

ABSTRACT

The research activity presented in this PhD Thesis aimed to analyse the numerous and various metrics proposed for the quantification of motor stability in human motion analysis.

Human motion analysis points to provide quantitative measures for the objective characterization of specific motion patterns, such as gait, with the aim to support evidence based clinical decision. In a biomechanical perspective, the quantification of joint kinematics and dynamics was demonstrated to be effective for the assessment of functional limitations associated with specific pathological conditions, of the effectiveness of surgical and rehabilitative procedures, and of prosthetic devices.

In recent years, the significant interest in finding effective methods for the quantification and prediction of fall risk in elderly subjects, due to its social and economical costs, led to a proliferation of novel metrics, applied to motion analysis data, for the quantification of locomotor stability.

The majority of these metrics originate from the theory of dynamical systems and have been used in robotics to design controllers. Thus, they have been applied to gait analysis data, assuming similar interpretability in terms of motor control, resulting in a large amount of published studies, often leading to not conclusive and sometimes contrasting results. This can be related to the lack of a methodological reference for the appropriate experimental assessment and implementation of these metrics (e.g. target variables, number of strides, sampling frequency, implementation parameters) and of a clear functional correlate, establishing the relationship between the metrics and their possible clinical interpretation (i.e. different metrics quantify different mathematical features of the analysed variable, which need to be related to specific characteristics of motor control).

Aiming to assess gait stability as an expression of motor control, both intrinsic properties of the human body and their relationship with the specific movement pattern

must be taken into account. To this purpose, non-linear metrics, such as Lyapunov Exponent, Recurrence Quantification Analysis, Harmonic Ratio, and Multiscale Sample Entropy, describing different aspects (e.g. stability, regularity, complexity) of gait pattern related to the motor control system (e.g. chaotic, stochastic, locally stable), were analysed.

The aim of this PhD dissertation was to improve the understanding of these non-linear metrics, providing evidence for the definition of methodological references for their experimental assessment, implementation, and possible clinical interpretation in specific conditions.

In particular:

- to provide correct and reliable acquisition, the harmonic content of trunk acceleration signal during gait was investigated, as well as the potential influence of reduced sampling frequency in the computation
- to guide experimental assessment, the potential influence of testing conditions (i.e. environment and test protocol), was analysed in young healthy adults
- to propose possible clinical interpretation in a specific clinical context, the analysed non-linear metrics were related to clinical rating scales in a sub-acute stroke population, providing an integrated clinical interpretation of specific motion characteristics.

Even though not exhaustive, the results of this research activity provide an essential set of basic knowledge for the definition of a reference for the reliable use and interpretation of these non-linear metrics.

SUMMARY

INTRODUCTION

Walkers are "practitioners of the city", for the city is made to be walked.
A city is a language, a repository of possibilities, and walking is the act of speaking that language, of selecting from those possibilities.
Just as language limits what can be said, architecture limits where one can walk, but the walker invents other ways to go.

Walking is how the body measures itself against the earth.
Rebecca Solnit, Wanderlust: A History of Walking

Interest in human motion goes back very far in human history, and it has been motivated by curiosity, needs and made possible by methods available at that time. The ancient Greek philosopher Aristotele (383 a.C. - 321 a.C.) published, besides many other fundamental works, also a (short) text ΠΕΡΙ ΠΟΡΕΙΑΣ ΖΩΙΩΝ [1] focusing on the gait of animals. Aristotele defined locomotion system as "*the parts that are useful to animals for movement in place*". This text is the first known document on biomechanics [2]. It already contains very detailed observations about the motion patterns of humans when involved in some particular activities. After that, art was definitely a major driving force for many centuries for specifying human motion (e.g. Leonardo da Vinci, Braune, and Fischer), but motion was only presented by means of static artwork. The first dynamic presentation of motion was through moving pictures, and this came nearly 2000 years later, at the end of the 19th century. Eadweard Muybridge (1830 - 1904), by a dispute that a galloping horse may have all four hooves off the ground, in 1878 set up a series of cameras for recording fast motion alongside a barn; his rapid sequence of photographs of a galloping horse showed all four hooves off the ground for part of the time [3,4]. His technique was applied to

different movement studies (e.g. walking, walking downstairs, boxing) becoming *de facto* the beginning of biomechanics of human motion.

Approaching the modern time, human motion analysis has modified its goals, from a simple observation and qualitative description to a quantitative and objective characterization of specific motion patterns, such as gait, with the aim to quantify performance, possible functional limitations, along with impairment and disability, and to support evidence based clinical decisions [5,6].

In a biomechanical perspective, the quantification of joint kinematics and dynamics was demonstrated to be effective for the assessment of functional limitations associated with specific pathological conditions or aging (i.e. risk of falling in elderly subjects), of the efficacy of surgical and rehabilitative procedures, and of prosthetic devices.

In recent years, the search for effective methods to quantify and predict fall risk in elderly subjects has risen particular interest in both research and clinical practice, since falls place a heavy economic burden on society, and are responsible for a considerable loss of life quality [7,8]. Proposals of novel metrics have proliferated for the quantification of locomotor stability from motion analysis data. These metrics originate from dynamical system theory (e.g. Lyapunov Exponents [9], Recurrence Quantification Analysis [10], and Poincaré Plots features [11]), frequency domain analysis (e.g. Harmonic Ratio [12], Index of Harmonicity [13]), and information theory (e.g. Sample Entropy). They quantify different signal features, aiming to characterize underlying system characteristics. For instance, Lyapunov Exponents and Recurrence Quantification Analysis are meant to evaluate the local stability and the nature (e.g. chaotic, stochastic) of the analysed system. Poincaré plot features address the variability of the analysed signal. Harmonic Ratio gives an indication of the regularity of the analysed signal trough the spectral analysis and, a sort of quantification of the complexity of the signal is evaluated by Sample Entropy (or Multiscale Sample Entropy on multiple spatio-temporal scales). These non-linear metrics, already applied in other contexts, such as robotics [14,15], have been widely used on gait analysis data, assuming similar interpretability in terms of motor control system.

Sample Entropy has been found to discriminate subjects of different ages [16], faller and non-faller elderlies [17] or pathological ones [18,19]. Despite of the promising results, these studies often lead to opposite conclusion i.e. higher entropy [17,18] *vs* lower entropy [16,20–22] associated to better health condition. These discrepancies could be due to different acquisition and measure parameters used (e.g. sampling frequency and coarse graining parameter).

Local dynamic stability during gait, quantified using largest Lyapunov Exponents [23], is meant to quantify locomotor stability. Although Lyapunov Exponents have shown to be related to risk of falling [20], and to discriminate different subjects' conditions [19–21,24–26], there is no common consensus on the implementation (e.g. parameters and variables [27] of the state space reconstruction), on experimental assessment (e.g. indoor walking, treadmill, free walking) and moreover, on data acquisition and processing (e.g. sampling frequency, data filtering).

Also the harmonic ratio presents several issues concerning its implementation and reliability. In the literature, several studies [12,28–32] applied harmonic ratio to different gait variables (e.g. trunk acceleration, head acceleration), and on different portions of signal (e.g. single stride [29], multiple strides [33,34]). Moreover, even applying the method to both the same variable and signal portion, the measure reliability is low [29]. This could be due to non-homogeneous acquisition, pre-processing, and task protocols used. The reported studies referred to different walking condition (e.g. walking straight or in circle), acquired with different sampling frequency (e.g. from 50 to 200 Hz) and implementing different pre-processing (e.g. filtered signal or unfiltered one).

From a methodological point of view, analysing relevant aspects associated with the specific experimental conditions is essential, since non-linear time series analysis often showed non-monotonic relationships due to intrinsic non-linear nature of the measure, even when applied in the same context [12,35]. Moreover, it is known that results of non-linear time series analysis of gait accelerations strongly depend on sensor placement [12].

The shortly reported literature review shows not conclusive and often contrasting results that can be associated with the lack of a methodological

reference for the appropriate experimental assessment and the implementation of these metrics (e.g. target variables, number of strides, sampling frequency, implementation parameters) and of a clear functional correlate, establishing the relationship between the metrics and their possible clinical interpretation (i.e. different metrics quantify different mathematical features of the analysed variable, which need to be related to specific characteristics of motor control).

The choice of the target signal variables should be driven by what the metrics are meant to provide, i.e. the quantification of locomotor stability in terms of motor control system interpretation. In general, human movements, as any other manifestation of biological systems, are investigated by analysing different specific characteristics (e.g. complexity, adaptability, regularity), often generalized as variability and stability.

On one hand, human movement variability can be defined as the typical variations that are present in motor performance and are observed across multiple repetitions of a task. Bernstein et al. [36] suggested that the same task may be accomplished with different motion patterns exploiting redundant degrees of freedom (e.g. different kinematics, loading conditions, muscle activation patterns). On the other hand, in dynamical systems, stability refers to a coordinative pattern's resilience to a change in response to a perturbation as measured by variance or deviation from the preferred or attractor state, or the ability to rapidly return to an attractor state [37]. Consequently, stability arises from the intrinsic properties of the model (e.g. masses, inertias, control system) and the specific movement pattern (e.g. gait) [38]. According to the above-mentioned concepts, the variability of gait is evaluated assessing changes in the peripheral realization of the pattern itself [38–41] (e.g. stride time data); whereas the stability of gait pattern should be assessed on a signal that is a summary of both the intrinsic properties of the human body and the specific movement pattern. Recent studies [40,42], assessing both healthy (from 4 year-old children to 25 year-old young adults) and pathological subjects (stroke), analysed the role of joint kinematics variability in relation to the stability of the centre of mass trajectory, approximated by the lower trunk [38,43,44]. They found that joint

kinematics variability lead to stabilize the lower trunk trajectory, suggesting that the lower trunk analysis can be used to track gait stability changes.

The aim of this PhD dissertation was to contribute to a better understanding of these non-linear metrics, when applied to trunk acceleration data during gait, providing evidence for methodological reference for their experimental assessment, implementation, and possible clinical interpretation in specific conditions.

Therefore, the present work starts with an overview of the non-linear stability measures used to quantify locomotor stability (Chapter 1). This first Chapter aims to illustrate the mathematical reference of the analysed metrics, highlighting the role of relevant parameters and the possible interpretation when applied in gait analysis.

From Chapter 2 to Chapter 4, relevant open issues about the definition of methodological references for the implementation and experimental assessment of the analysed non-linear metrics have been addressed. To this end:

- the harmonic content of trunk acceleration signal during gait of nine age groups from 7 to 85 year-old was analysed (Chapter 2)
- it was assessed if and how a reduced sampling frequency (from 128 Hz to 42.6 Hz) influences the computation of the analysed non-linear metrics (Chapter 3)
- the potential influence of testing conditions (i.e. environment and test protocol) was analysed in young healthy adults (Chapter 4)

Finally, in Chapter 5 the possible clinical interpretation of the proposed metrics was investigated in a sub-acute stroke population, analysing the relationship between the proposed novel metrics, describing gait characteristics, and an extended selection of clinical rating scales.

REFERENCES:

[1] On the Motion of Animals, (n.d.). https://ebooks.adelaide.edu.au/a/aristotle/motion/ (accessed December 11, 2017).

[2] R. Klette, G. Tee, Understanding Human Motion: A Historic Review, CITR, The University of Auckland, New Zealand, 2007. https://researchspace.auckland.ac.nz/handle/2292/2778 (accessed December 11, 2017).

[3] R. Sklar, A world history of film, Harry N. Abrams, 2002.

[4] B. Rosenhahn, R. Klette, D. Metaxas, Human Motion: Understanding, Modelling, Capture, and Animation, Springer Science & Business Media, 2008.

[5] M.G. Benedetti, E. Beghi, A. De Tanti, A. Cappozzo, N. Basaglia, A.G. Cutti, A. Cereatti, R. Stagni, F. Verdini, M. Manca, S. Fantozzi, C. Mazzà, V. Camomilla, I. Campanini, A. Castagna, L. Cavazzuti, M. Del Maestro, U.D. Croce, M. Gasperi, T. Leo, P. Marchi, M. Petrarca, L. Piccinini, M. Rabuffetti, A. Ravaschio, Z. Sawacha, F. Spolaor, L. Tesio, G. Vannozzi, I. Visintin, M. Ferrarin, SIAMOC position paper on gait analysis in clinical practice: General requirements, methods and appropriateness. Results of an Italian consensus conference, Gait Posture. 58 (2017) 252–260. doi:10.1016/j.gaitpost.2017.08.003.

[6] A. Castagna, M. Rabuffetti, A. Montesano, M. Ferrarin, Role of gait analysis in the process of clinical decision making concerning post-stroke patients, Gait Posture. 33 (2011) S20–S21. doi:10.1016/j.gaitpost.2010.10.027.

[7] S. Heinrich, K. Rapp, U. Rissmann, C. Becker, H.-H. König, Cost of falls in old age: a systematic review, Osteoporos. Int. 21 (2009) 891–902. doi:10.1007/s00198-009-1100-1.

[8] B. Homann, A. Plaschg, M. Grundner, A. Haubenhofer, T. Griedl, G. Ivanic, E. Hofer, F. Fazekas, C.N. Homann, The impact of neurological disorders on the risk for falls in the community dwelling elderly: a case-controlled study, BMJ Open. 3 (2013). doi:10.1136/bmjopen-2013-003367.

[9] J.B. Dingwell, H.G. Kang, Differences Between Local and Orbital Dynamic Stability During Human Walking, J. Biomech. Eng. 129 (2006) 586–593. doi:10.1115/1.2746383.

[10] C.L. Webber, J.P. Zbilut, Dynamical assessment of physiological systems and states using recurrence plot strategies, J. Appl. Physiol. 76 (1994) 965–973.

[11] M. Brennan, M. Palaniswami, P. Kamen, Do existing measures of Poincare plot geometry reflect non-linear features of heart rate variability?, IEEE Trans. Biomed. Eng. 48 (2001) 1342–1347. doi:10.1109/10.959330.

[12] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration patterns of the head and pelvis when walking on level and irregular surfaces, Gait Posture. 18 (2003) 35–46. doi:10.1016/S0966-6362(02)00159-5.

[13] C.J.C. Lamoth, P.J. Beek, O.G. Meijer, Pelvis–thorax coordination in the transverse plane during gait, Gait Posture. 16 (2002) 101–114. doi:10.1016/S0966-6362(01)00146-1.

[14] S.J. Guastello, D.E. Nathan, M.J. Johnson, Attractor and Lyapunov models for reach and grasp movements with application to robot-assisted therapy, Non-linear Dyn. Psychol. Life Sci. 13 (2009) 99–121.

[15] M. Monirul Islam, K. Murase, Chaotic dynamics of a behavior-based miniature mobile robot: effects of environment and control structure, Neural Netw. 18 (2005) 123–144. doi:10.1016/j.neunet.2004.09.002.

[16] M.C. Bisi, R. Stagni, Complexity of human gait pattern at different ages assessed using multiscale entropy: From development to decline, Gait Posture. 47 (2016) 37–42. doi:10.1016/j.gaitpost.2016.04.001.

[17] E.A.F. Ihlen, A. Weiss, A. Bourke, J.L. Helbostad, J.M. Hausdorff, The complexity of daily life walking in older adult community-dwelling fallers and non-fallers, J. Biomech. 49 (2016) 1420–1428. doi:10.1016/j.jbiomech.2016.02.055.

[18] Y. Tochigi, N.A. Segal, T. Vaseenon, T.D. Brown, Entropy Analysis of Tri-Axial Leg Acceleration Signal Waveforms for Measurement of Decrease of Physiological Variability in Human Gait, J. Orthop. Res. 30 (2012) 897–904. doi:10.1002/jor.22022.

[19] C.J. Lamoth, F.J. van Deudekom, J.P. van Campen, B.A. Appels, O.J. de Vries, M. Pijnappels, Gait stability and variability measures show effects of impaired cognition and dual tasking in frail people, J. Neuroengineering Rehabil. 8 (2011) 2. doi:10.1186/1743-0003-8-2.
[20] M.C. Bisi, F. Riva, R. Stagni, Measures of gait stability: performance on adults and toddlers at the beginning of independent walking, J. NeuroEngineering Rehabil. 11 (2014). doi:10.1186/1743-0003-11-131.
[21] F. Riva, M.J.P. Toebes, M. Pijnappels, R. Stagni, J.H. van Dieën, Estimating fall risk with inertial sensors using gait stability measures that do not require step detection, Gait Posture. 38 (2013) 170–174. doi:10.1016/j.gaitpost.2013.05.002.
[22] G. Leverick, T. Szturm, C.Q. Wu, Using Entropy Measures to Characterize Human Locomotion, J. Biomech. Eng. 136 (2014) 121002–121002. doi:10.1115/1.4028410.
[23] M.T. Rosenstein, J.J. Collins, C.J. De Luca, A practical method for calculating largest Lyapunov exponents from small data sets, Phys. Non-linear Phenom. 65 (1993) 117–134. doi:10.1016/0167-2789(93)90009-P.
[24] M.J.P. Toebes, M.J.M. Hoozemans, R. Furrer, J. Dekker, J.H. van Dieën, Local dynamic stability and variability of gait are associated with fall history in elderly subjects, Gait Posture. 36 (2012) 527–531. doi:10.1016/j.gaitpost.2012.05.016.
[25] C.J.C. Lamoth, E. Ainsworth, W. Polomski, H. Houdijk, Variability and stability analysis of walking of transfemoral amputees, Med. Eng. Phys. 32 (2010) 1009–1014. doi:10.1016/j.medengphy.2010.07.001.
[26] E.A.F. Ihlen, A. Weiss, Y. Beck, J.L. Helbostad, J.M. Hausdorff, A comparison study of local dynamic stability measures of daily life walking in older adult community-dwelling fallers and non-fallers, J. Biomech. 49 (2016) 1498–1503. doi:10.1016/j.jbiomech.2016.03.019.
[27] D. Hamacher, D. Hamacher, N.B. Singh, W.R. Taylor, L. Schega, Towards the assessment of local dynamic stability of level-grounded walking in an older population, Med. Eng. Phys. 37 (2015) 1152–1155. doi:10.1016/j.medengphy.2015.09.007.
[28] T. Doi, S. Hirata, R. Ono, K. Tsutsumimoto, S. Misu, H. Ando, The harmonic ratio of trunk acceleration predicts falling among older people: results of a 1-year prospective study, J. NeuroEngineering Rehabil. 10 (2013) 7. doi:10.1186/1743-0003-10-7.
[29] I. Pasciuto, E. Bergamini, M. Iosa, G. Vannozzi, A. Cappozzo, Overcoming the limitations of the Harmonic Ratio for the reliable assessment of gait symmetry, J. Biomech. 53 (2017) 84–89. doi:10.1016/j.jbiomech.2017.01.005.
[30] J.L. Bellanca, K.A. Lowry, J.M. VanSwearingen, J.S. Brach, M.S. Redfern, Harmonic ratios: A quantification of step to step symmetry, J. Biomech. 46 (2013) 828–831. doi:10.1016/j.jbiomech.2012.12.008.
[31] K.A. Lowry, N. Lokenvitz, A.L. Smiley-Oyen, Age- and speed-related differences in harmonic ratios during walking, Gait Posture. 35 (2012) 272–276. doi:10.1016/j.gaitpost.2011.09.019.
[32] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration Patterns of the Head and Pelvis When Walking Are Associated With Risk of Falling in Community-Dwelling Older People, J. Gerontol. A. Biol. Sci. Med. Sci. 58 (2003) M446–M452. doi:10.1093/gerona/58.5.M446.
[33] J. Howcroft, J. Kofman, E.D. Lemaire, W.E. McIlroy, Analysis of dual-task elderly gait in fallers and non-fallers using wearable sensors, J. Biomech. 49 (2016) 992–1001. doi:10.1016/j.jbiomech.2016.01.015.
[34] F. Riva, M.C. Bisi, R. Stagni, Gait variability and stability measures: Minimum number of strides and within-session reliability, Comput. Biol. Med. 50 (2014) 9–13. doi:10.1016/j.compbiomed.2014.04.001.
[35] F. Riva, M.C. Bisi, R. Stagni, Orbital stability analysis in biomechanics: A systematic review of a non-linear technique to detect instability of motor tasks, Gait Posture. 37 (2013) 1–11. doi:10.1016/j.gaitpost.2012.06.015.
[36] N.A. Bernshteĭn, The co-ordination and regulation of movements, Pergamon Press, Oxford; New York, 1967. http://books.google.com/books?id=F9dqAAAAMAAJ (accessed December 2, 2017).

[37] R.E.A. van Emmerik, S.W. Ducharme, A.C. Amado, J. Hamill, Comparing dynamical systems concepts and techniques for biomechanical analysis, J. Sport Health Sci. 5 (2016) 3–13. doi:10.1016/j.jshs.2016.01.013.
[38] S.M. Bruijn, O.G. Meijer, P.J. Beek, J.H. van Dieën, Assessing the stability of human locomotion: a review of current measures, J. R. Soc. Interface. 10 (2013). doi:10.1098/rsif.2012.0999.
[39] D. Hamacher, N.B. Singh, J.H. Van Dieën, M.O. Heller, W.R. Taylor, Kinematic measures for assessing gait stability in elderly individuals: a systematic review, J. R. Soc. Interface. 8 (2011) 1682–1698. doi:10.1098/rsif.2011.0416.
[40] E. Papi, P.J. Rowe, V.M. Pomeroy, Analysis of gait within the uncontrolled manifold hypothesis: Stabilisation of the centre of mass during gait, J. Biomech. 48 (2015) 324–331. doi:10.1016/j.jbiomech.2014.11.024.
[41] J.B. Dingwell, J. John, J.P. Cusumano, Do humans optimally exploit redundancy to control step variability in walking?, PLoS Comput. Biol. 6 (2010) e1000856. doi:10.1371/journal.pcbi.1000856.
[42] M.C. Bisi, R. Stagni, Is CoM kinematics a descriptive parameter of gait motor development? Verification on children and adults, Gait Posture. 42 (2015) S100. doi:10.1016/j.gaitpost.2015.06.182.
[43] W. Zijlstra, A.L. Hof, Displacement of the pelvis during human walking: experimental data and model predictions, Gait Posture. 6 (1997) 249–262. doi:10.1016/S0966-6362(97)00021-0.
[44] K. Wilmut, W. Du, A.L. Barnett, Gait patterns in children with Developmental Coordination Disorder, Exp. Brain Res. 234 (2016) 1747–1755. doi:10.1007/s00221-016-4592-x.

Chapter 1

NON-LINEAR METRICS FOR THE CHARACTERIZATION OF HUMAN LOCOMOTION

Mathematics is the language with which God wrote the universe
Galileo Galilei

1. NON-LINEAR METRICS FOR THE CHARACTERIZATION OF HUMAN LOCOMOTION

1.1 INTRODUCTION

In recent years, the significant interest in finding effective methods for the quantification and prediction of fall risk in elderly subjects, has led to a proliferation of novel metrics proposals, to be applied to motion analysis data, in particular gait, for the quantification of locomotor stability [1–8].

These metrics, already applied in other contexts [9,10], have been widely used on gait analysis data, assuming similar interpretability in terms of motor control system. Among these, in this dissertation, the metrics, which had demonstrated the best performance in terms of reliability, usability and specificity (e.g. stability, regularity, complexity, harmonicity) of gait as related to motor control (e.g. chaotic, stochastic, locally stable) according to literature[1] [1,2,4–6,8,11], were selected. In particular, *Recurrence Quantification Analysis* (RQA) and *Lyapunov Exponent* (LE) [12], already applied in robotics and originated from a *non-linear analysis* methods based on a *dynamical systems theory*, analyse the time domain of the employed signal. They give an indication about, the nature (i.e. chaos, stochastic, noisy signal) and the stability of the observed dynamic system. *Harmonic Ratio* (HR) [13], proposed to assess the harmonic content of the signal, analyses the frequency domain giving ad indication about the regularity and harmonicity of the employed signal. Moreover, from the field of *information theory* the concept of *entropy,* through the *Sample Entropy* (SEN) [14] measure, has been used to evaluate the *complexity* of the signal.

[1] Literature published before April 2015

In this Chapter an overview of the mathematical base of the above-mentioned non-linear indexes, with particular attention to their applicability in gait analysis (e.g. tuning of parameters) were discussed.

1.2 INDEXES DERIVED FROM THE DYNAMICAL SYSTEM APPROACH

The term *system* generally refers to a certain portion of the physical world, which is the object of the observation. The terms *dynamic* and *dynamical* are generally used to describe systems that evolve or change over time. Consequently, a dynamic system is completely defined by a set of variables called *state variables*, which evolve over the time, and by the rules/laws namely *state equations* that describe the observed temporal evolution [15].

The *state-space* is the collection of all possible state variables values. Curves in state-space are known as the *state trajectories* and from its study is possible to determine the *structural characteristics* (e.g. node point, limit cycle, toroid, and more in general N-dimensional attractors) of the system. The importance and utility of the state-space clearly appears.

On one hand, for the systems that can be mathematically modelled the state-space is known from the state equations, consequently its dimension is equal to the number of state variables (or state equation due to the Rouché-Capelli theorem). On the other hand, in all the case in which the equations of the system are unknown, such as generically the biological system and so the motor control system, a time series can be used to reconstruct the attractor of the underlying dynamic process [16].

1.2.1 STATE-SPACE RECONSTRUCTION

The *state-space reconstruction* from a time series is a powerful approach for the analysis of the complex non-linear systems, widespread in the natural and human word. This is a very important step to identify the structural characteristics of the time series and it is also necessary in the calculus of the Recurrence Quantification Analysis, Lyapunov Exponent, and other non-linear tools.

The *embedding transformation*, based on the *Takens' theorem* (1981) [16] that provides the conditions under which a smooth attractor can be reconstructed from the observations, aims to transform a time series, which has one dimension, into a higher dimensional space in order to create the state-space underling the observed system.

The minimum number of required variables in order to create a valid state-space from a given time series is called *embedding dimension;* in this space the true structures of the observed system are completely contained.

In order to obtain the reconstructed state-space shifted time versions of the original time series are used.

In particular, given a time series $X = \{x_1 \dots x_N\}$, a time (or number of sample) delay (lag) used as shift and an embedding dimension (eD) the reconstructed state-space (SS_i^r) is composed by vectors ss_i^r described by the equation 1.1

$$ss_i^r = \{x_1, \dots, x_{N-(eD-i)*lag}\} \qquad i = 1, \dots eD \tag{1.1}$$

Follows

$$SS_i^r = \{ss_1^r, \dots, ss_i^r, \dots, ss_{eD}^r\} \qquad i = 1, \dots eD \tag{1.2}$$

The reconstructed state-space depends from the time delay (lag) and from the embedding dimension (eD).

Time delay

In order to find an appropriate value of the time delay (lag) it is important to understand the meaning of this parameter.

Each state-space contains the information of the system at a specific time. A vector, x_i should contain the information about the system at time i and, x_{i+lag} should contain the information about the system at time $i + lag$. Therefore finding an appropriate delay means to find the value that gives new information about the system that could not be obtained from the previous state-space. On one hand, if the time delay is too small the information obtained from the state-space at time $i + lag$ is almost the same extracted from the pervious state-space at time i. On the other hand, if the time delay is too large, although the two state-space provide different information, a lot of information could be lost between them. Therefore, the relationship between x_i and x_{i+lag} is to be quantified.

In the literature [17,18], two methods have been proposed aiming to address this issue: the *zero crossing of the autocorrelation function* and the *first minimum of the average mutual information*.

The autocorrelation function evaluates only linear relationship (and not non-linear ones) between the shifted time series; this could be a criticality due to the intrinsic non-linear nature of the motor control system.

To evaluate non-linear relationship average mutual information can be used [19,20]; indeed it can be interpreted as the non-linear version of the autocorrelation function [21].

If the first minimum of the average mutual information occurs for a time delay of 1 means that there is non correlation among the data; if this behaviour persists in all the employed data set it is possible conclude that the data are very noisy. Instead, if the average mutual information does not display a minimum, all the data points are strongly correlated to each other and consequently it is no possible know new information from different point of the state-space.

In these research studies (Chapters 3, 4, and 5), the first minimum of the average mutual information algorithm has been applied in order to identify the time delay used in the state-space reconstruction. The time delay was set to 10

samples, that using a sample frequency at 128 Hz means a time delay of 0.078 s. This choice is also in according with other studies [6,22–26] that evaluate trunk acceleration data during gait.

Even thought time delay value dramatically affects the shape attractor, it is not clear the impact in the calculus of metrics derived from the attractor itself [17]. For this reason the determination of the time delay has to be performed paying attention to, in particular, two factors: first, as above discussed, the algorithm choice that have to be driven by the linear (autocorrelation function) or non-linear (mutual information) nature of the observed system; second the influence of the sampling frequency. It goes without saying that the time delay and the corresponding number of samples are in relation with the used sampling frequency; moreover if the spectral analysis of the signal identifies that the used sampling frequency is unnecessary too high, shifted versions of the signal can be strongly correlated, and no time delay could be found. However, down-sampling the data could be a reliable processing in order to identify a time delay more appropriate [17]. This highlights the importance to identify and use a correct sampling frequency: not using an unnecessary high sampling frequency just to obtain more data points.

Embedding Dimension

Usually the term *dimension* means a measure to describe the size of an object: length, width, and height. A 3-dimensional object like a cube in a 2-dimensional space is wrongly identified with a square rather than line depending from the chosen plain; consequently, the true shape of a object is revealed when it is exanimated in a higher-dimensional space or where the dimensionality is equal to the true dimensions of the observed object.

Considering that a time series is an object in its state-space (i.e. its emergent attractor) and, as for the objects, the time series should be observed in a higher-dimensional space in order to identify its true structure, otherwise hidden in a lower-dimensional space. It follows that the determination of the embedding dimension is crucial to identify the right shape of the attractor.

In the literature, a general method to find an appropriate embedding dimension has been proposed. This involves the calculus of dynamic invariant (e.g. correlation dimension, Lyapunov Exponent) for successive embedding dimensions [27]: the appropriate embedding dimension is find when increasing the embedding dimension no changes in the dynamic invariant are observed. However one of the main drawbacks of this approach is the computational cost required to reconstruct the spate-space for increasing embedding dimensions. To address this issue the *false nearest neighbour algorithm* was proposed, becoming the most commonly used method to determine the embedding dimension [28,29]. This approach is based on eliminating false projections that occur when the space dimension is not large enough to unfold the dynamics of the attractor [28,30].

In this dissertation, an embedding dimension of 5 samples, using the *false nearest neighbour algorithm*, was found for all the directions of the trunk acceleration signal during gait accordingly with others studies [6,22–26,31].

1.2.2 RECURRENCE QUANTIFICATION ANALYSIS

The *Recurrence Quantification Analysis* (RQA) is a non-linear method for data analysis that quantifies the number and duration of *recurrences* (or neighbours) *points* of the analysed dynamical system presented in its (reconstructed) state-space trajectory [32]. It does not assume data stationary, and more in general it places no restrictions both on the statistical distribution of data and on data set length.

RQA is based on the analysis of particular features of the recurrence plots, including a quantification of deterministic structure and of non-stationarity [18,32,33]; it was developed by Zbilut and Webber Jr. [18,32] and extended, including measures of complexity [34].

Over the past decades, recurrence plot has proven to be valuable data visualization and analysis tools in the theoretical study of complex, time-varying dynamical systems as well as in various applications in biology, neuroscience,

biomechanics, psychology, physiology, engineering, physics, geosciences, linguistics, finance, economics, and other disciplines [30].

RQA algorithm consists in 3 main steps:

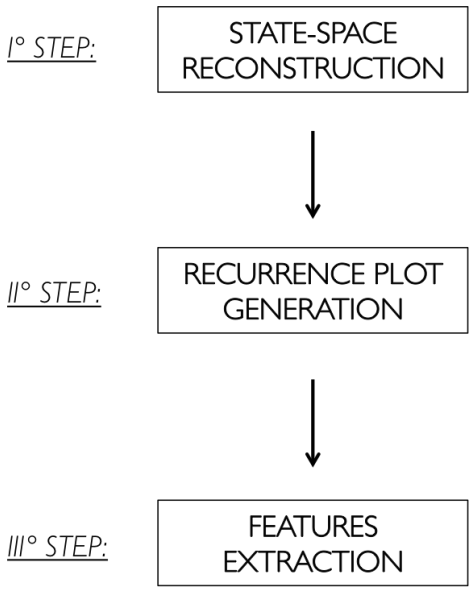

Figure 1: Flowchart of Recurrence Quantification Analysis.

Once the state-space is reconstructed (detailed above-mentioned) the next step is to create the *recurrence plot*. Here the *recurrence points*, namely points separated in time but which are (spatial) neighbours in the reconstructed state-space reflecting the evolution of the observed dynamics (as time progresses) [26], are identified. Simply, the recurrence plot reveals all the times when the state-space trajectory of the dynamical system visits roughly the same area in the state-space. In order to obtain the recurrence plot the distance between all the points of the embedded time series have to be calculated. If this distance is less than or equal to a threshold, *radius* (r), the point is a recurrence. It clearly appears that RQA required several input parameters: time delay and embedding dimension, used for the state-space reconstruction, and radius (r). For time delay (lag) and embedding dimension (eD) choice see the above-mentioned details. As concerns the radius (r), it has to be carefully tuned, indeed, if it is too low (r=0) only the exactly matching points would be considered recurrent, and this would be

expected only for ideal mathematical examples. Instead, if radius (r) is too high all the points would be considered recurrent suppressing the variance of the observed measure [26]. Radius (r) in this PhD dissertation was chosen at 40% of the maximum distance between data points in the embedding state-space in order to minimize the floor and ceil effects [18].

The third and last step is the features extraction. In literature several features have been proposed in order to evaluate different system characteristics (e.g. periodicity, random and stochastic behaviour, noise component, complexity, chaos) [26,31,35].

In this dissertation (Chapter 3, 4, and 5) the analysed features of the recurrence plot were: *Recurrence Rate* (RR), *Determinism* (DET), *Average Length of Diagonal Line* (AvgL).

Recurrence Rate (RR) is the number of recurrent points in the recurrence plot expressed as a percentage of the number of possibly recurrent points. It is the percentage of points within a distance r of one another. The obtained RR values for a given time series will depend on the used r values [18,26,34–36]. Mathematically speaking, the number of recurrent points delineates the number of embedded vector pairs near each other in N-dimensional space; meaning that embedded processes manifesting periodic dynamics have higher recurrence values than other embedded processes characterized by aperiodic dynamics [18]. In other words, RR gives an indication about how often a trajectory visits similar locations (points) in the state-space.

Determinism (DET) is the percentage of recurrent points which fall on upward diagonal line segments. DET will depend on the specified definition of the number of points forming a line segment. This is usually set as four consecutive recurrent points [31]. This is an extremely important variable, since it distinguishes between recurrent points that are individually dispersed and those that are organized into specific diagonal patterns. DET reflects the degree of determinism because, upward diagonal line segments indicate that the system is revisiting the same region of the attractor (or of the reconstructed space)

repeatedly; consequently it is related to the predictability of the dynamic system. In particular, DET relates to how often the trajectory re-visits similar state space locations ("shape"); the higher DET the more regular is the dynamic structure of the data [18,37].

Average Length of Diagonal Line (AvgL) is the average upward diagonal line length, where the diagonal lines are defined following determinism definition. AvgL indicates how long the repeated trajectory "lasts", this can be interpreted as the duration of the most repeated "shape". It is related to the velocity in the execution of the test (i.e. higher AvgL is expected for slower gait), but this duration is not independent from the regularity of the pattern (i.e. the gait is slower because each stride on average is slower) [31,37].

From the literature [5,31,36,38] it is possible conclude that higher RR and DET more regular is the dynamic of the dynamical structure of the system namely the motor control system. Moreover, AvgL is related to the task execution velocity [31,37]. RQA features (RR, DET, AvgL) have been shown to promising correlation with clinical scale, in a sub-acute stroke population [37], and also RQA were found to be positively associated with fall history [5]. RQA could hence represent useful tools in the identification of subjects for fall prevention programs [5] and to complement the standard clinical gait assessment [37]. Additionally, Bisi et al. [38] suggested that RQA better discern gait stability differentiating not only between unstable toddlers and stable healthy adults, but also evidencing the expected trend of the toddlers towards a higher stability with walking experience, and indicating elderly subjects as stable as or less stable than young adults.

1.2.3 LYAPUNOV EXPONENT

Lyapunov Exponent (LE) has been one of the most popular techniques used to evaluate the *local stability* in a dynamical system. It has been widely used for the analysis of various biological systems such as human gait [8,39–41], postural sway [42–44] and handwriting [45], due to the unnecessary exhibition of a discernable periodic structure, and therefore it does not exploit the pseudo-periodicity of some motor tasks [17].

The local stability of a dynamical system characterizes whether nearby (i.e., perturbed) points of a orbits will remain in a neighbourhood of that orbit or be repelled away from it, quantifying how the system state responds to very small (local) perturbations continuously in real time [12]. The exponential trend has been shown to approximate the moving away (i.e. divergence or convergence) from orbits [12,27,46,47].

Lyapunov Exponent is defined as the average exponential rate of divergence or convergence of nearby orbits (trajectory) in the state-space. It is common to focus only on the largest LE [40,46,48,49], it determines the fastest divergence exponential evolution. Positive exponents indicate local instability, with larger exponents indicating greater sensitivity to local perturbations.

Rosenstain et al. [47] provided a method to estimate the average exponential divergence (i.e. Lyapunov Exponent), for an embedded time series. The algorithm can be summarized as follows:

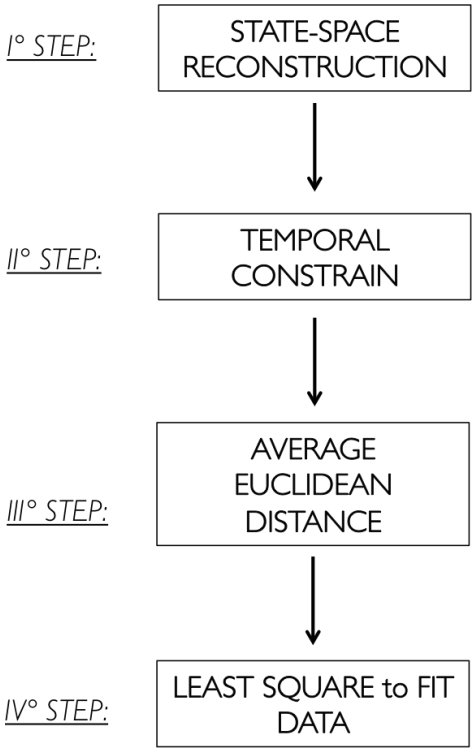

Figure 2: Flowchart Lyapunov Exponent algorithm

In particular, Euclidean distances between neighbouring trajectories in state-space were computed as a function of time and averaged over all original pairs of initially nearest neighbours. Lyapunov Exponents (λ) were estimated from the slopes of linear fits to these exponential divergence curves:

$$y(i) = \frac{1}{\Delta t}\langle ln\left[d_j(i)\right]\rangle \qquad (1.3)$$

where $d_j(i)$ was the Euclidean distance between the jth pair of initially nearest neighbours after i discrete time steps (i.e. $i\Delta t$ seconds) and $\langle * \rangle$ denotes the average over all values of j [47].

These local divergence curves always exhibited positive divergence reflecting the natural variability and intrinsic noise of the biological system

[42,46,48]. For chaotic systems, the local divergence would be linear, reflecting a constant exponential rate of divergence [47], and the slope of that line would approximate the maximum Lyapunov Exponent for the system. Since the obtained curves were clearly not linear [46], no basis for defining a true Lyapunov Exponent for human walking were found [42]. Nevertheless, these local divergence exponents have shown to provide a metrics for estimating the sensitivity of human walking to small intrinsic perturbations [46].

Lyapunov Exponent can be calculated over some finite time interval. In the local dynamical stability of gait finite time interval of 1 stride and of 6 strides have been proposed. In particular, *short-term Lyapunov Exponent* λ_S was calculated from the slope of linear fit to the divergence curve between 0 and 1 stride and *long-term Lyapunov Exponent* λ_L was calculated as the slope between the 4^{th} and 10^{th} strides.

Using Rosenstain et al. [47] method, the LE calculation (short-term and long-term) principally depends on the parameters used for the state-space reconstruction [47]. These aspects are well explained in the first part of this Chapter. Moreover, in this dissertation the LE were calculated using four different state-space: one composed by the three acceleration directions (antero-posterior medio-lateral and vertical) of the trunk and three composed by the delay embedding (eD = 5 and lag = 10) of each trunk acceleration components.

Several studies using Rosenstein et al [47] approach for the calculation of LE have been presented in literature [25,46,50–54]. However, the systematic review proposed by Riva et al. [11] concluded that all subjects always showed a significant degree of local instability during locomotion, even though no subject ever fell or stumbled during the tests, and no association were found between Lyapunov Exponents and fall risk [55]. Moreover, Bisi et al [23,24,38] founded that short-term Lyapunov Exponents were able to discern between toddler and adult groups, in particular increasing of age population corresponds a decreasing of instability.

1.3 INDEXES DERIVED FROM FREQUENCY DOMAIN

Frequency-domain analysis is one of the most important tools in signal processing applications. While time-domain analysis shows how a signal changes over time, frequency-domain analysis shows how the signal's energy is distributed over a range of frequencies. A frequency-domain representation also includes information on the phase shift that must be applied to each frequency component in order to recover the original time signal with a combination of all the individual frequency components.

A signal can be converted between the time and frequency domains with a pair of mathematical operators called a transform. An example is the *Fourier Transform*, which decomposes a function into the sum of a (potentially infinite) number of sine wave frequency components. The frequency-domain representation of a signal carries information about the signal's magnitude and phase at each frequency. The *spectrum frequency* is the frequency domain representation of the signal [56].

Among novel metrics proposals for the quantification of locomotor stability several of them *directly* or *indirectly* analyse the harmonic content of the signal. On one hand, the direct analysis of the spectrum usually implies the calculation of the Fourier Transform or of the power spectrum density: as Harmonic Ratio [13], used to quantify regularity. On the other hand, the harmonic content of the signal affects metrics when identifying specific features that are calculated from different filtered versions of the original signal, such as Multiscale Sample Entropy (MSE) [14], an assessment of the complexity of the signal at different time-scales. In particular MSE merges the knowledge of the *information theory* with a *multiscale approach* (see Chapter 1.3.2).

1.3.1 HR

The *Harmonic Ratio* (HR) is an index based on the spectral analysis here applied on the lower trunk accelerations signal.

Mathematically, Harmonic Ratio (HR) is calculated by decomposing the antero-posterior (AP), vertical (V), and medio-lateral (ML) acceleration directions signal into harmonics using a discrete Fourier transform [13]. The summed amplitudes of the first 10 even harmonics are divided by the summed amplitudes of the first 10 odd harmonics for the AP and V acceleration directions, and vice-versa for the ML accelerations. This difference is due to the fact that whereas the AP accelerations have two periods every stride, showing a dominance of the second harmonic, representing step frequency (i.e. two times the fundamental frequency) and subsequent even harmonics, ML accelerations have only one period per stride, reflecting a dominance of the first (i.e. fundamental frequency) and subsequent odd harmonics [13].

Although, this index is widely used in gait analysis [6,38,57–61] there is no common standard implementation. The main discrepancies, which arise from the literature, concern: the choice of the signal portion on which calculating the index that means both step-by-step [58] and the entire acceleration signal collected over several strides [4–6,38,62], and the identification of the fundamental frequency, HR parameter [13]. Regarding the evaluation of the fundamental frequency, this can be performed either in the time domain, as the inverse of the mean stride time, or in the frequency domain as the frequency corresponding to the maximum of the Fourier Transform acceleration modulus (see Chapter 4 for more details).

In this dissertation HR was calculated on the entire signal and the fundamental frequency was obtained trough the frequency domain.

A higher HR is an indication of increased regularity of gait, which can be interpreted as increased stability. Bisi et al. [38] suggested that HR better discern gait stability differentiating not only between unstable toddlers and stable healthy adults, but also evidencing the expected trend of the toddlers towards a higher

stability with walking experience, and indicating elderly subjects as stable as or less stable than young adults.

1.3.2 MSE

Carnot (1824), as first in classical thermodynamics, developed the concept of *Entropy* (EN). He defined entropy as a state function that quantifies the energy in a system that cannot be used to performed work. Later, Boltzman (1896) gave further insights into the concept of entropy, by using probability theory to describe entropy on a molecular scale.

Later, the concept of entropy has been also used in the field of *information theory*. *Shannon entropy* (1948) is defined as the loss of information in a time series or signal. It is based on what it is known about the current states of the system and how well the next state can be predicted. If a system has very low entropy, the next state of the system is very predictable, *vice versa* if a system has very high entropy.

The *Sample Entropy* (SEN) [63] derived from the *Approximated Entropy*, developed by Pincus et al. [64] with the intention to be used in the analysis of experimental time series data generated by biological process.

Mathematically, SEN reflects the conditional probability that two sequences of m consecutive data points, which are similar to each other, will remain similar when one more consecutive point is included. Being "similar" means that the value of a specific measure of distance (e.g. Euclidean, Chebyshev) is less than a threshold (r) [14].

SEN provides a measure of unpredictability or irregularity of the time series that should not be always interpreted as complexity: a very periodic signal and a highly random one are both very low in complexity, but have different SEN values [17,37]. However, in motion analysis, SEN can be considered a measure of how much the acquired trunk acceleration deviates from the cyclic nature of gait

and, therefore, in this context it is common practice to interpret SEN as a measure of complexity [14,22,63].

Multiscale Sample Entropy (MSE) has been introduced, by Costa et al.[14], to quantify the complexity (i.e. sample entropy, SEN) of a time series on multiple spatio-temporal scales.

The multiscale approach consists into create consecutive coarse-grained time version of the original time series. Given a time series, $X = \{x_1, \dots, x_N\}$, the constructed consecutive coarse-grained version are obtained by averaging a successively increasing number of data points in a non overlapping windows as shown in Figure 3.

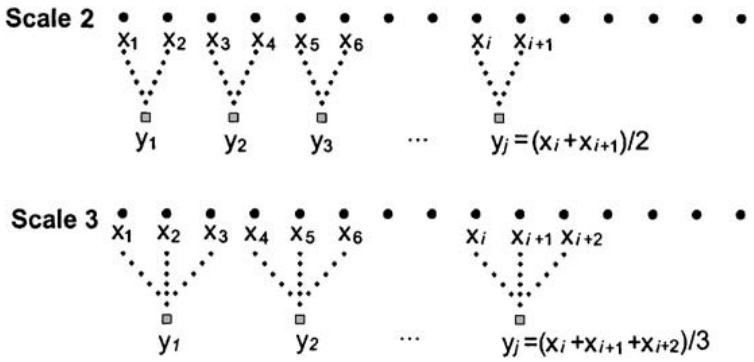

Figure 3: Schematic illustration of the coarse-graining procedure for scales 2 and 3 [14].

Each element of the coarse-grained time series, $y_i^{(\tau)}$ is calculated accordingly to the equation:

$$y_i^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i \qquad (1.4)$$

where τ represents the scale factor and $1 \leq j \leq {}^{N}/_{\tau}$. The length of each coarse-grained time series is ${}^{N}/_{\tau}$. For scale 1, the coarse-grained time series is simply the original one. Then for each one of the coarse-grained time series the SEN could be calculated obtained the Multiscale Sample Entropy (MSE).

The effects of the coarse graining procedure could be interpreted as a sort of moving average (low pass) filter. Indeed, the obtained coarse-grained time series

setting τ i.e. 2 has no zero frequency content below $f_s/2$ Hz, where f_s is the sampling frequency of the original time series. In general, a coarse-grained time series have frequency content different to zero below f_s/τ Hz.

Therefore, MSE is a function of m and r (derived from the calculus of SEN) and τ (due to the coarse grain procedure) parameters, but is largely independent by the time series length when the total number of data points is larger than approximately 750 samples [63,65].

Costa et al. [14] found that MSE is not very dependent on the specific values of m and r. Instead particular attention has to be paid in τ tuning. The frequency content of the coarse-grained signal will be dependent not only from the chosen τ but also from the sampling frequency of the original time series. Thus, only MSE values obtained with both same τ and sampling frequency or a same combination of these two parameters (f_s and τ) should be compared, in this manner the frequency content of the coarse-grained analysed series will be equal. Moreover, τ has to be chosen coherently and consistently with the frequency content of the analysed signal.

In this dissertation m=2, r=0.2 and τ ranging from 1 to 6 were used.

In biomechanics, MSE and/or SEN have been applied to evaluate gait stability and were found to be promising quantitative methods for evaluating fall risk in elderly and/or pathologic subjects [5,22,38,66–68]. Leverick et al. [66] found that SEN measures experienced statistically significant increases in response to increasing age and gait impairment caused by cognitive interference on healthy adults and elderlies. Bisi et al. [38] evaluated the performance of different gait stability indexes on young adults and toddlers at the onset of walking (toddlers were assumed as individuals whose gait is a priori unstable) and found that SEN was able to differentiate between unstable toddlers and stable healthy individuals. In another study Bisi et al. [22] demonstrated that MSE complexity is a relevant parameter of gait development during life, decreasing from immature to mature gait and then increasing again during old age.

1.4 REFERENCES

[1] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration Patterns of the Head and Pelvis When Walking Are Associated With Risk of Falling in Community-Dwelling Older People, J. Gerontol. A. Biol. Sci. Med. Sci. 58 (2003) M446–M452. doi:10.1093/gerona/58.5.M446.

[2] J.M. Hausdorff, D.A. Rios, H.K. Edelberg, Gait variability and fall risk in community-living older adults: A 1-year prospective study, Arch. Phys. Med. Rehabil. 82 (2001) 1050–1056. doi:10.1053/apmr.2001.24893.

[3] L. Bizovska, Z. Svoboda, N. Vuillerme, M. Janura, Multiscale and Shannon entropies during gait as fall risk predictors—A prospective study, Gait Posture. 52 (2017) 5–10. doi:10.1016/j.gaitpost.2016.11.009.

[4] F. Riva, E. Grimpampi, C. Mazza, R. Stagni, Are gait variability and stability measures influenced by directional changes?, Biomed. Eng. OnLine. 13 (2014) 56. doi:10.1186/1475-925X-13-56.

[5] F. Riva, M.J.P. Toebes, M. Pijnappels, R. Stagni, J.H. van Dieën, Estimating fall risk with inertial sensors using gait stability measures that do not require step detection, Gait Posture. 38 (2013) 170–174. doi:10.1016/j.gaitpost.2013.05.002.

[6] F. Riva, M.C. Bisi, R. Stagni, Gait variability and stability measures: Minimum number of strides and within-session reliability, Comput. Biol. Med. 50 (2014) 9–13. doi:10.1016/j.compbiomed.2014.04.001.

[7] E.A.F. Ihlen, A. Weiss, Y. Beck, J.L. Helbostad, J.M. Hausdorff, A comparison study of local dynamic stability measures of daily life walking in older adult community-dwelling fallers and non-fallers, J. Biomech. 49 (2016) 1498–1503. doi:10.1016/j.jbiomech.2016.03.019.

[8] D. Hamacher, D. Hamacher, N.B. Singh, W.R. Taylor, L. Schega, Towards the assessment of local dynamic stability of level-grounded walking in an older population, Med. Eng. Phys. 37 (2015) 1152–1155. doi:10.1016/j.medengphy.2015.09.007.

[9] S.J. Guastello, D.E. Nathan, M.J. Johnson, Attractor and Lyapunov models for reach and grasp movements with application to robot-assisted therapy, Nonlinear Dyn. Psychol. Life Sci. 13 (2009) 99–121.

[10] M. Monirul Islam, K. Murase, Chaotic dynamics of a behavior-based miniature mobile robot: effects of environment and control structure, Neural Netw. 18 (2005) 123–144. doi:10.1016/j.neunet.2004.09.002.

[11] F. Riva, M.C. Bisi, R. Stagni, Orbital stability analysis in biomechanics: A systematic review of a nonlinear technique to detect instability of motor tasks, Gait Posture. 37 (2013) 1–11. doi:10.1016/j.gaitpost.2012.06.015.

[12] J.B. Dingwell, H.G. Kang, Differences Between Local and Orbital Dynamic Stability During Human Walking, J. Biomech. Eng. 129 (2006) 586–593. doi:10.1115/1.2746383.

[13] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration patterns of the head and pelvis when walking on level and irregular surfaces, Gait Posture. 18 (2003) 35–46. doi:10.1016/S0966-6362(02)00159-5.

[14] M. Costa, C.-K. Peng, A. L. Goldberger, J.M. Hausdorff, Multiscale entropy analysis of human gait dynamics, Phys. Stat. Mech. Its Appl. 330 (2003) 53–60. doi:10.1016/j.physa.2003.08.022.

[15] R.C. Hilborn, Chaos and Nonlinear Dynamics: An Introduction for Scientists and Engineers, Oxford University Press, 2000.

[16] L. Noakes, The takens embedding theorem, Int. J. Bifurc. Chaos. 01 (1991) 867–872. doi:10.1142/S0218127491000634.

[17] N. Stergiou, Nonlinear Analysis for Human Movement Variability, CRC Press, 2016.

[18] C.L. Webber, J.P. Zbilut, Dynamical assessment of physiological systems and states using recurrence plot strategies, J. Appl. Physiol. 76 (1994) 965–973.

[19] A.M. Fraser, Reconstructing attractors from scalar time series: A comparison of singular system and redundancy criteria, Phys. Nonlinear Phenom. 34 (1989) 391–404. doi:10.1016/0167-2789(89)90263-7.

[20] A.M. Fraser, H.L. Swinney, Independent coordinates for strange attractors from mutual information, Phys. Rev. A. 33 (1986) 1134–1140. doi:10.1103/PhysRevA.33.1134.
[21] W. Li, Mutual information functions versus correlation functions, J. Stat. Phys. 60 (1990) 823–837. doi:10.1007/BF01025996.
[22] M.C. Bisi, R. Stagni, Complexity of human gait pattern at different ages assessed using multiscale entropy: From development to decline, Gait Posture. 47 (2016) 37–42. doi:10.1016/j.gaitpost.2016.04.001.
[23] M.C. Bisi, R. Stagni, Development of gait motor control: what happens after a sudden increase in height during adolescence?, Biomed. Eng. OnLine. 15 (2016). doi:10.1186/s12938-016-0159-0.
[24] M.C. Bisi, R. Stagni, Evaluation of toddler different strategies during the first six-months of independent walking: A longitudinal study, Gait Posture. 41 (2015) 574–579. doi:10.1016/j.gaitpost.2014.11.017.
[25] T.E. Lockhart, J. Liu, Differentiating fall-prone and healthy adults using local dynamic stability, Ergonomics. 51 (2008) 1860–1872. doi:10.1080/00140130802567079.
[26] M.A. Riley, R. Balasubramaniam, M.T. Turvey, Recurrence quantification analysis of postural fluctuations, Gait Posture. 9 (1999) 65–78. doi:10.1016/S0966-6362(98)00044-7.
[27] A. Wolf, J.B. Swift, H.L. Swinney, J.A. Vastano, Determining Lyapunov exponents from a time series, Phys. Nonlinear Phenom. 16 (1985) 285–317. doi:10.1016/0167-2789(85)90011-9.
[28] M.B. Kennel, R. Brown, H.D.I. Abarbanel, Determining embedding dimension for phase-space reconstruction using a geometrical construction, Phys. Rev. A. 45 (1992) 3403–3411. doi:10.1103/PhysRevA.45.3403.
[29] Analysis of Observed Chaotic Data | Henry D.I. Abarbanel | Springer, n.d. //www.springer.com/gp/book/9780387983721 (accessed December 14, 2017).
[30] Recurrence Quantification Analysis - Theory and Best | Charles L. Webber, Jr. | Springer, n.d. //www.springer.com/la/book/9783319071541 (accessed November 27, 2017).
[31] F. Sylos Labini, A. Meli, Y.P. Ivanenko, D. Tufarelli, Recurrence quantification analysis of gait in normal and hypovestibular subjects, Gait Posture. 35 (2012) 48–55. doi:10.1016/j.gaitpost.2011.08.004.
[32] C.L. Webber, J.P. Zbilut, Assessing Deterministic Structures in Physiological Systems Using Recurrence Plot Strategies, in: Bioeng. Approaches Pulm. Physiol. Med., Springer, Boston, MA, 1996: pp. 137–148. doi:10.1007/978-0-585-34964-0_8.
[33] C.L. Webber, Rhythmogenesis of Deterministic Breathing Patterns, in: Rhythms Physiol. Syst., Springer, Berlin, Heidelberg, 1991: pp. 177–191. doi:10.1007/978-3-642-76877-4_14.
[34] N. Marwan, N. Wessel, U. Meyerfeldt, A. Schirdewan, J. Kurths, Recurrence-plot-based measures of complexity and their application to heart-rate-variability data, Phys. Rev. E Stat. Nonlin. Soft Matter Phys. 66 (2002) 026702. doi:10.1103/PhysRevE.66.026702.
[35] X. Li, G. Ouyang, X. Yao, X. Guan, Dynamical characteristics of pre-epileptic seizures in rats with recurrence quantification analysis, Phys. Lett. A. 333 (2004) 164–171. doi:10.1016/j.physleta.2004.10.028.
[36] S. Ramdani, G. Tallon, P.L. Bernard, H. Blain, Recurrence Quantification Analysis of Human Postural Fluctuations in Older Fallers and Non-fallers, Ann. Biomed. Eng. 41 (2013) 1713–1725. doi:10.1007/s10439-013-0790-x.
[37] P. Tamburini, D. Mazzoli, R. Stagni, Towards an objective assessment of motor function in sub-acute stroke patients: Relationship between clinical rating scales and instrumental gait stability indexes, Gait Posture. 59 (2018) 58–64. doi:10.1016/j.gaitpost.2017.09.033.
[38] M.C. Bisi, F. Riva, R. Stagni, Measures of gait stability: performance on adults and toddlers at the beginning of independent walking, J. NeuroEngineering Rehabil. 11 (2014). doi:10.1186/1743-0003-11-131.
[39] U.H. Buzzi, N. Stergiou, M.J. Kurz, P.A. Hageman, J. Heidel, Nonlinear dynamics indicates aging affects variability during gait, Clin. Biomech. 18 (2003) 435–443. doi:10.1016/S0268-0033(03)00029-9.
[40] N. Stergiou, C. Moraiti, G. Giakas, S. Ristanis, A.D. Georgoulis, The effect of the walking speed on the stability of the anterior cruciate ligament deficient knee, Clin. Biomech. 19 (2004) 957–963. doi:10.1016/j.clinbiomech.2004.06.008.

[41] C.J. Lamoth, F.J. van Deudekom, J.P. van Campen, B.A. Appels, O.J. de Vries, M. Pijnappels, Gait stability and variability measures show effects of impaired cognition and dual tasking in frail people, J. Neuroengineering Rehabil. 8 (2011) 2. doi:10.1186/1743-0003-8-2.
[42] J. Timmer, S. Haussler, M. Lauk, C.-H. Lucking, Pathological tremors: Deterministic chaos or nonlinear stochastic oscillators?, Chaos Woodbury N. 10 (2000) 278–288. doi:10.1063/1.166494.
[43] R.T. Harbourne, N. Stergiou, Nonlinear analysis of the development of sitting postural control, Dev. Psychobiol. 42 (2003) 368–377. doi:10.1002/dev.10110.
[44] C.J.C. Lamoth, R.C. van Lummel, P.J. Beek, Athletic skill level is reflected in body sway: A test case for accelometry in combination with stochastic dynamics, Gait Posture. 29 (2009) 546–551. doi:10.1016/j.gaitpost.2008.12.006.
[45] M. Longstaff, R. Heath, A nonlinear analysis of the temporal characteristics of handwriting, Hum. Mov. Sci. (1999) 485–524. doi:10.1016/S0167-9457(99)00028-7.
[46] J.B. Dingwell, J.P. Cusumano, Nonlinear time series analysis of normal and pathological human walking, Chaos Interdiscip. J. Nonlinear Sci. 10 (2000) 848–863. doi:10.1063/1.1324008.
[47] M.T. Rosenstein, J.J. Collins, C.J. De Luca, A practical method for calculating largest Lyapunov exponents from small data sets, Phys. Nonlinear Phenom. 65 (1993) 117–134. doi:10.1016/0167-2789(93)90009-P.
[48] J.B. Dingwell, J.P. Cusumano, D. Sternad, P.R. Cavanagh, Slower speeds in patients with diabetic neuropathy lead to improved local dynamic stability of continuous overground walking, J. Biomech. 33 (2000) 1269–1277. doi:10.1016/S0021-9290(00)00092-0.
[49] R.T. Harbourne, N. Stergiou, Movement Variability and the Use of Nonlinear Tools: Principles to Guide Physical Therapist Practice, Phys. Ther. 89 (2009) 267–282. doi:10.2522/ptj.20080130.
[50] J.B. Dingwell, L.C. Marin, Kinematic variability and local dynamic stability of upper body motions when walking at different speeds, J. Biomech. 39 (2006) 444–452. doi:10.1016/j.jbiomech.2004.12.014.
[51] K.P. Granata, S.A. England, Stability of Dynamic Trunk Movement, Spine. 31 (2006) E271–E276. doi:10.1097/01.brs.0000216445.28943.d1.
[52] S.A. England, K.P. Granata, The influence of gait speed on local dynamic stability of walking, Gait Posture. 25 (2007) 172–178. doi:10.1016/j.gaitpost.2006.03.003.
[53] J.B. Dingwell, J.P. Cusumano, P.R. Cavanagh, D. Sternad, Local Dynamic Stability Versus Kinematic Variability of Continuous Overground and Treadmill Walking, J. Biomech. Eng. 123 (2000) 27–32. doi:10.1115/1.1336798.
[54] A.D. Segal, M.S. Orendurff, J.M. Czerniecki, J.B. Shofer, G.K. Klute, Local dynamic stability in turning and straight-line gait, J. Biomech. 41 (2008) 1486–1493. doi:10.1016/j.jbiomech.2008.02.012.
[55] D. Hamacher, N.B. Singh, J.H. Van Dieën, M.O. Heller, W.R. Taylor, Kinematic measures for assessing gait stability in elderly individuals: a systematic review, J. R. Soc. Interface. 8 (2011) 1682–1698. doi:10.1098/rsif.2011.0416.
[56] V. Williams, A. Bruton, C. Ellis-Hill, K. McPherson, What really matters to patients living with chronic obstructive pulmonary disease? An exploratory study, Chron. Respir. Dis. 4 (2007) 77–85. doi:10.1177/1479972307078482.
[57] T. Doi, S. Hirata, R. Ono, K. Tsutsumimoto, S. Misu, H. Ando, The harmonic ratio of trunk acceleration predicts falling among older people: results of a 1-year prospective study, J. NeuroEngineering Rehabil. 10 (2013) 7. doi:10.1186/1743-0003-10-7.
[58] I. Pasciuto, E. Bergamini, M. Iosa, G. Vannozzi, A. Cappozzo, Overcoming the limitations of the Harmonic Ratio for the reliable assessment of gait symmetry, J. Biomech. 53 (2017) 84–89. doi:10.1016/j.jbiomech.2017.01.005.
[59] J.L. Bellanca, K.A. Lowry, J.M. VanSwearingen, J.S. Brach, M.S. Redfern, Harmonic ratios: A quantification of step to step symmetry, J. Biomech. 46 (2013) 828–831. doi:10.1016/j.jbiomech.2012.12.008.
[60] K.A. Lowry, N. Lokenvitz, A.L. Smiley-Oyen, Age- and speed-related differences in harmonic ratios during walking, Gait Posture. 35 (2012) 272–276. doi:10.1016/j.gaitpost.2011.09.019.

[61] C. Mazzà, M. Iosa, F. Pecoraro, A. Cappozzo, Control of the upper body accelerations in young and elderly women during level walking, J. NeuroEngineering Rehabil. 5 (2008) 30. doi:10.1186/1743-0003-5-30.
[62] J. Howcroft, J. Kofman, E.D. Lemaire, W.E. McIlroy, Analysis of dual-task elderly gait in fallers and non-fallers using wearable sensors, J. Biomech. 49 (2016) 992–1001. doi:10.1016/j.jbiomech.2016.01.015.
[63] J.S. Richman, J.R. Moorman, Physiological time-series analysis using approximate entropy and sample entropy, Am. J. Physiol. - Heart Circ. Physiol. 278 (2000) H2039–H2049.
[64] S.M. Pincus, Approximate entropy as a measure of system complexity., Proc. Natl. Acad. Sci. U. S. A. 88 (1991) 2297–2301.
[65] J.M. Yentes, N. Hunt, K.K. Schmid, J.P. Kaipust, D. McGrath, N. Stergiou, The Appropriate Use of Approximate Entropy and Sample Entropy with Short Data Sets, Ann. Biomed. Eng. 41 (2013) 349–365. doi:10.1007/s10439-012-0668-3.
[66] G. Leverick, T. Szturm, C.Q. Wu, Using Entropy Measures to Characterize Human Locomotion, J. Biomech. Eng. 136 (2014) 121002–121002. doi:10.1115/1.4028410.
[67] Y. Tochigi, N.A. Segal, T. Vaseenon, T.D. Brown, Entropy Analysis of Tri-Axial Leg Acceleration Signal Waveforms for Measurement of Decrease of Physiological Variability in Human Gait, J. Orthop. Res. 30 (2012) 897–904. doi:10.1002/jor.22022.
[68] E.A.F. Ihlen, A. Weiss, A. Bourke, J.L. Helbostad, J.M. Hausdorff, The complexity of daily life walking in older adult community-dwelling fallers and non-fallers, J. Biomech. 49 (2016) 1420–1428. doi:10.1016/j.jbiomech.2016.02.055.

Chapter 2

GAIT TRUNK ACCELERATION: CHARACTERIZATION OF THE SPECTRUM FROM DEVELOPMENT TO DECLINE[1]

Information is the resolution of uncertainty.
Claude Shannon

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2. GAIT TRUNK ACCELERATION: CHARACTERIZATION OF THE SPECTRUM FROM DEVELOPMENT TO DECLINE

2.1 ABSTRACT

Acquisition and processing of trunk acceleration signal during gait have assumed a key role in motor assessment. This has led to the development of different indexes and metrics to evaluate gait performances that, directly or indirectly, imply the analysis of the harmonic content of the signal. The knowledge of the spectrum characteristics of the trunk acceleration signal during gait is crucial to identify hardware and software requirements and to correctly use the indexes and their parameters. The aim of this study was to characterize the spectrum of humans gait at different ages: from 7 to 85 years old. To do this, the fundamental frequency and the frequency corresponding to the 50, 90, 95 and 98% of the normalized power of the trunk acceleration during gait were analysed. Results highlighted that: the harmonic content (at 98%) of the acceleration signal for all the analysed population, with exception of the adolescents, is below 30 Hz and the highest frequency contribute is associated to the AP direction. In adolescents, spectrum is wide up to 45 Hz.

Keys words: *Frequency analysis, fundamental frequency, gait, gait signal bandwidth, stride frequency.*

2.2 INTRODUCTION

ABBREVIATIONS

7YC	7-years old children
9YC	9-years old children
15YAf	15-years old adolescents Female Not Grown
15YAm_NG	15-years old adolescents Male Not Grown
15YAm_G	15-years old adolescents Male Grown
25YA	25-years old adults
45YA	45-years old adults
65YA	65-years old adults
85YE	85-years old elderlies
AP	Antero-posterior direction
ML	Medio-lateral
V	Vertical
$\mathbf{f_s}$	Sampling frequency
FF	Fundamental Frequency
$\mathbf{FF_{NORM}}$	Normalized Fundamental Frequency
$\mathbf{f_{50\%ap,ml,v}}$	Frequency corresponding to the 50% of the normalized power of trunk acceleration in the three directions
$\mathbf{f_{90\%ap,ml,v}}$	Frequency corresponding to the 90% of the normalized power of trunk acceleration in the three directions
$\mathbf{f_{95\%ap,ml,v}}$	Frequency corresponding to the 95% of the normalized power of trunk acceleration in the three directions
$\mathbf{f_{98\%ap,ml,v}}$	Frequency corresponding to the 98% of the normalized power of trunk acceleration in the three directions

In recent years, due to the development and advance in commercial wearable inertial measurement units (IMUs), accelerometric measures have become extensively used for the functional characterization of gait in both healthy (e.g. children, adolescents, adults, elderly) and pathologic (e.g. Parkinson, Stroke) subjects [1–5].

Accelerometric measures collected at different sites (often lower trunk, but also head, upper trunk, ankle, wrist) have been used to calculate a number of parameters characterizing gait functions and performance. Among these, the most common are probably gait temporal parameters (i.e. toe off, heel strike, stride time, cadence, step time), but also spatial parameters (i.e. stride length) [6–9], and more or less complex metrics proposed to quantify different properties of gait and related motor control, such as variability, stability, complexity, and regularity [10–12].

A number of different methods and algorithms have been proposed to calculate these parameters and indexes, often based on very different approaches (e.g. for gait temporal parameters: thresholds, features, frequency analysis, similarity models). Nevertheless, most of these algorithms directly or indirectly analyse the harmonic content of the signal. On one hand, the direct analysis of the spectrum usually implies the calculation of the Fourier Transform or of the power spectrum density, as, for instance, to calculate Harmonic Ratio [13] and Index of Harmonicity [14], used to quantify regularity. On the other hand, the harmonic content of the signal may affect metrics when identifying specific features that are calculated from different filtered versions of the original signal, such as Multiscale Sample Entropy [15], used to assess complexity at different time-scales.

In addition to these processing aspects, smart devices (e.g. smartphones Android or iOS based) seem to be revolutionizing gait analysis. Indeed, the use of smartphones with embedded accelerometers has offered new opportunities for clinicians and researchers to easily and relatively inexpensively record and characterize gait in detail [7,8,16]. Moreover they have also been proposed as portable devices allowing continuous and/or pervasive monitoring of gait, also in pathologic populations [17,18] aimed to be effective for the assessment of functional limitations associated with specific pathological conditions, of the powerfulness of surgical and rehabilitative procedures.

Although this approach is extremely interesting and opens a number of possible applications, some technical aspects have still to be better analysed.
Several studies [19,16,20–23] showed that features computed on the signal that is acquired with smart devices are comparable to the ones obtained from the traditional accelerometers, maintaining the same acquisition parameters (e.g. sampling frequency). However, these commercial devices, due to multiple functions provided, currently do not support constant sampling frequencies (i.e. main acquisition parameter) higher than 50 Hz (for a android systems) that is significantly lower than what is usually adopted in reference research studies (higher than 100 Hz) [17].

Even though in literature several studies [24–28] characterized a set of signal features in time, frequency, and time-frequency domains, to extract clinically valuable information from gait accelerometer signals, none of them analysed specifically the spectrum characteristics of the gait acceleration signal. This is surprising, considering the relevance of spectrum characteristics for the proper design of signal acquisition and processing.

What is lacking is a characterization of the harmonic content of gait acceleration signal with reference values of parameters that allow to perform a reliable and coherent, with the observed task and population, design of signal acquisition and processing.

Recalling the signal theory, the most characterizing parameters are the fundamental frequency (i.e. the greatest common divisor of all the frequency components contained in the signal), and the bandwidth, (i.e. frequency range in which the signal's spectral density is nonzero or above an arbitrary threshold value), at different percentage of signal's power. Moreover, frequency resolution of the signal spectrum, that is the capacity to discriminate two near frequency components in the spectrum, influences the accuracy of all the given values parameters. Thus, frequency resolution, which depends from the time duration of the assessed signal, has to be carefully managed.

The present study was designed to partially fill this gap, characterizing the harmonic content of the acceleration signal of lower trunk during gait in populations from 7 to 85 years of age. The acceleration of lower trunk was addressed in particular, because it is assumed to approximate the acceleration of the centre of mass, describing the typical inverse pendulum mechanics, characterizing human natural gait [29]. Measures of lower trunk acceleration were extensively used to calculate gait spatio-temporal parameters [7,30,31] quantify gait performance, stability, and fall risk in elderly and pathologic subjects [32–34], and describe gait performance and maturation in populations of different ages [11,35,36].

The aim of this study was to characterize the spectrum of humans gait at different ages: from 7 to 85 years old. To do this fundamental frequency, frequency corresponding to the 50%, 90%, 95% and 98% of the signal power

were assessed, taking in to account the appropriate gait trunk acceleration signal spectrum resolution.

2.3 MATERIALS and METHODS

2.3.1 Participants

Nine age groups (7 to 85 years of age) of 10 healthy subjects each were included in the study. Group details are shown in Table 1.

All participants had no known developmental delay or reported musculoskeletal pathology. Adolescents (15 years of age) were divided in 3 groups to isolate the possible influence of gender and growth spurt on motor performance, as reported by Bisi et al [36]. Group 15YAm_G included 10 male adolescents, who had a growth spurt in the previous 3 months; group 15YAm_NG included 10 male adolescents, who had no growth spurt in the previous 3 months; group 15YAf included 10 female adolescents, none of the female adolescents had a growth spurt in the period of observation. Anthropometric characteristics did not show any statistical significant differences from adolescent (all groups) to elderly.

The Review Board Committee of the authors' institution approved the study, and informed consent was obtained from adult participants and from the participants' parents for children.

POPULATION	ACRONYM	AGE [year]	WEIGHT [kg]	HEIGHT [cm]
7-years old children	7YC	7 (7, 7)	29 (22, 37)	129 (119, 134)
9-years old children	9YC	9 (9, 9)	34 (22,45)	140 (138,145)
15-years old adolescents Female Not Grown	15YAf	15 (15,15)	54 (49, 74)	162 (147, 172)
15-years old adolescents Male Not Grown	15YAm_NG[a]	15 (15,15)	64 (49, 74)	172 (169,176)
15-years old adolescents Male Grown	15YAm_G[a]	15 (15,15)	59 (46, 65) Δw=2 (-1, 4)	172 (160,175) Δh=3.6 (3, 4)
25-years old adults	25YA	25 (22, 26)	70 (48, 86)	168 (154, 187)
45-years old adults	45YA	45 (41, 48)	74 (45, 100)	174 (155, 193)

POPULATION	ACRONYM	AGE [year]	WEIGHT [kg]	HEIGHT [cm]
65-years old adults	65YA	65 (62, 69)	85 (68, 120)	176 (164,186)
85-years old elderlies	85YE	85 (84, 91)	74 (57, 90)	177 (160, 175)

Table 1: Details of age groups: median, minimum and maximum values.

2.3.2 Experimental setup

Two tri-axial wireless inertial sensor (OPAL, Apdm USA) were fixed: one on the lower back at L5 level using elastic belt, orienting the three axes along the antero-posterior (AP), vertical (V) and medio-lateral (ML) body directions, and one above the ankle for the stride detection [31].

The participants walked at self-selected speed for about 30 seconds along a straight path free from obstacles and distractions. Trunk acceleration was recorded with a sampling frequency (f_s) at 128 Hz.

2.3.3 Data analysis

First, for all the subjects, an integer number of strides to cover at least a time duration of 20 seconds of the acquired acceleration signal were analysed, excluding the first 5 and the final 3 or more seconds, to avoid gait initiation and termination phases. The number of analysed strides raged from 23 (7YC) to 14 (15YAf). Maximal signal duration was 21.3 s.

The analysis of an integer number of strides was required for coherent sampling, and the minimum duration of 20 seconds to guarantee a frequency resolution of 0.05 Hz [37].

Unfiltered data were analysed to assure that information was not lost and/or modified by the filtering process. The only performed pre-processing was to remove the mean value and/or linear trend from all the components of the acceleration signal.

Stationary of the trunk acceleration signal of each subject in all the three directions was tested and verified using the method described by Bendat, J. S. et al., [38]: a non-parametric approach, that makes no basic assumptions about the nature of the system and does not assume that the data are normally distributed

[39].

The following features on trunk acceleration were computed for all subjects:

Fundamental Frequency FF (2.1):

$$FF = \frac{\max_{f\in[0,f_S/2]}\left|dft(\sqrt{acc_{AP}{}^2+acc_{ML}{}^2+acc_V{}^2})\right|^2}{2} \qquad (2.1)$$

where dft is the Discrete Fourier Transform, computed using the Fast Fourier Transform algorithm, of the trunk acceleration signal module.

The frequency corresponding to the 50, 90, 95 and 98% of the normalized power of trunk acceleration in the three directions ($f_{50,90,95,98\%_{ap,ml,v}}$) (2.2):

$$f_{50,90,95,98\%_{ap,ml,v}} = \left\{ f \in \left[0,\frac{f_S}{2}\right] \middle| \min\left(\frac{comulative_{psd_{ap,ml,v}}}{PW_{tot_{ap,ml,v}}}\% - 50,90,95,98\%\right)\right\} \qquad (2.2)$$

To avoid influence of the anthropometric parameters, the fundamental frequency was normalized FF_{NORM} [40]. Whereas, in order to assess possible interference between the harmonic content and the fundamental frequency, all the other features were normalized ($f_{50,90,95,98\%_{ap,ml,v_{NORM}}}$) with respect to the fundamental frequency.

A Jarque-Bera test [41] was performed to verify the normal distribution of the calculated features on the different groups. Since the normal distribution was not verified on all the groups, median, 25- and 75-percentile values were calculated. In order to evaluate how precisely the median value of the analysed age groups approximated the median value of the corresponded population, the confidence interval (CI) at 95% was calculated for each feature and age group. Data processing and statistical analysis were implemented in Matlab 2015b (MathWorks BV, USA).

2.4 RESULTS

All the 50th, 25th, and 75th percentile values of the analysed features (normalized and not normalized) were included in the corresponding CI with a level of significance 5% (CI at 95%).

2.4.1 Fundamental Frequency

FF ranged from a maximum of 1.1 Hz, for the 7 year-old (7YC), to a minimum of 0.88 Hz for the male grown adolescents (15YAm_G).

In particular, FF decreased from 7YC to all 15YA group, increased for 25YA and then showed similar values from 45YA to 85YE.

The normalized fundamental frequency FF_{NORM} showed a different trend with respect to FF. Similar values (0.30) from 7YC to 15YA were found, with exception of the adolescent not grown male that showed the lowest value (0.26). Instead, from 25YA (0.32) to 85YE (0.29) FF_{NORM} values decreased.

In Figure 1 the median 25- and 75-percentile, for FF and FF_{NORM} -panel A and B respectively- for all the populations were presented.

2.4.2 $f_{50,90,95,98\%_{ap}}$: harmonic content in AP direction.

The frequency corresponding to the 50% of the normalized power of the trunk acceleration in AP direction ranged from a maximum value of 4.5 Hz for 15YAm_NG to a minimum value of 2.03 Hz for 85YE.

$f_{90,95,98\%_{ap}}$ showed similar values for all populations with exception of all the adolescent groups, which exhibited higher values. Similar results were found for the normalized features.

2.4.3 $f_{50,90,95,98\%_{ml}}$: harmonic content in ML direction.

No trend was observed for all features in ML direction.

$f_{50\%_{ml}}$ ranged from 4.96 Hz (45YA) to 8.31 Hz (9YC), $f_{90\%_{ml}}$ from 10.16

Hz (45YA) to 12.91 (15YAf), $f_{95\%_{ml}}$ from 13.04 Hz (45YA) to 16.38 (15YAm_NG) and $f_{98\%_{ml}}$ from 17.12 (25YA) to 20.01 (65YA).

2.4.4 $f_{50,90,95,98\%_v}$: harmonic content in V direction.

$f_{50\%_v}$ showed similar values for all groups, with a maximum value (3.49 Hz) for 15YAm_G and a minimum value (1.97 Hz) for 45YA.

Increasing the percentage of normalized power (from 90% to 98%) the trend becomes more pronounced: 7YC, 9YC, 25YA and 45YA show similar values, while the remaining groups -all adolescents, 65YA and 85YE- show higher values than the other populations, but close to each other. The same results were found for the normalized features.

Median, 25- and 75-percentile values of all the features -not normalized and normalized- in AP and V direction are reported in Figure 2. Grey tones become darker from $f_{50\%}$ to $f_{98\%}$.

Detailed values (median, 25- and 75-percentile) of each feature (FF, FF_{NORM}, $f_{50,90,95,98\%_{ap,ml,v}}$ and $f_{50,90,95,98\%_{ap,ml,v_{NORM}}}$) in all directions (AP, ML and V) can be found in the supplementary material.

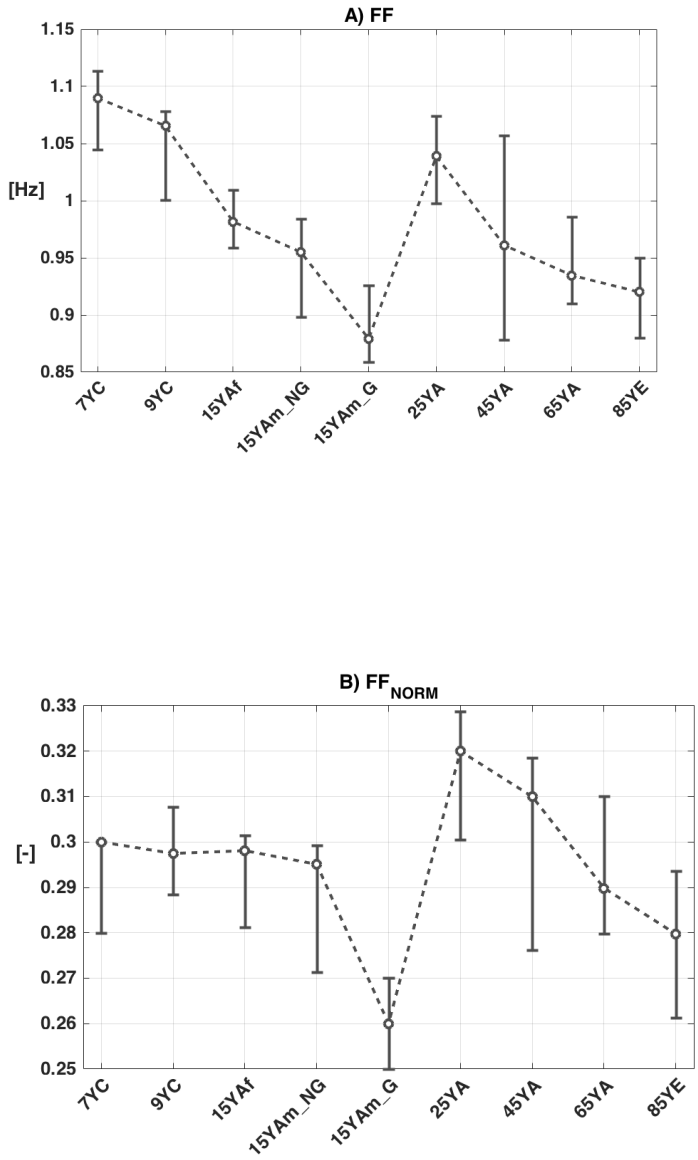

Figure 1: Median, 25- and 75-percentile of fundamental frequency (FF) and normalized fundamental frequency (FF_{NORM}), panel A and B respectively, for all the age groups.

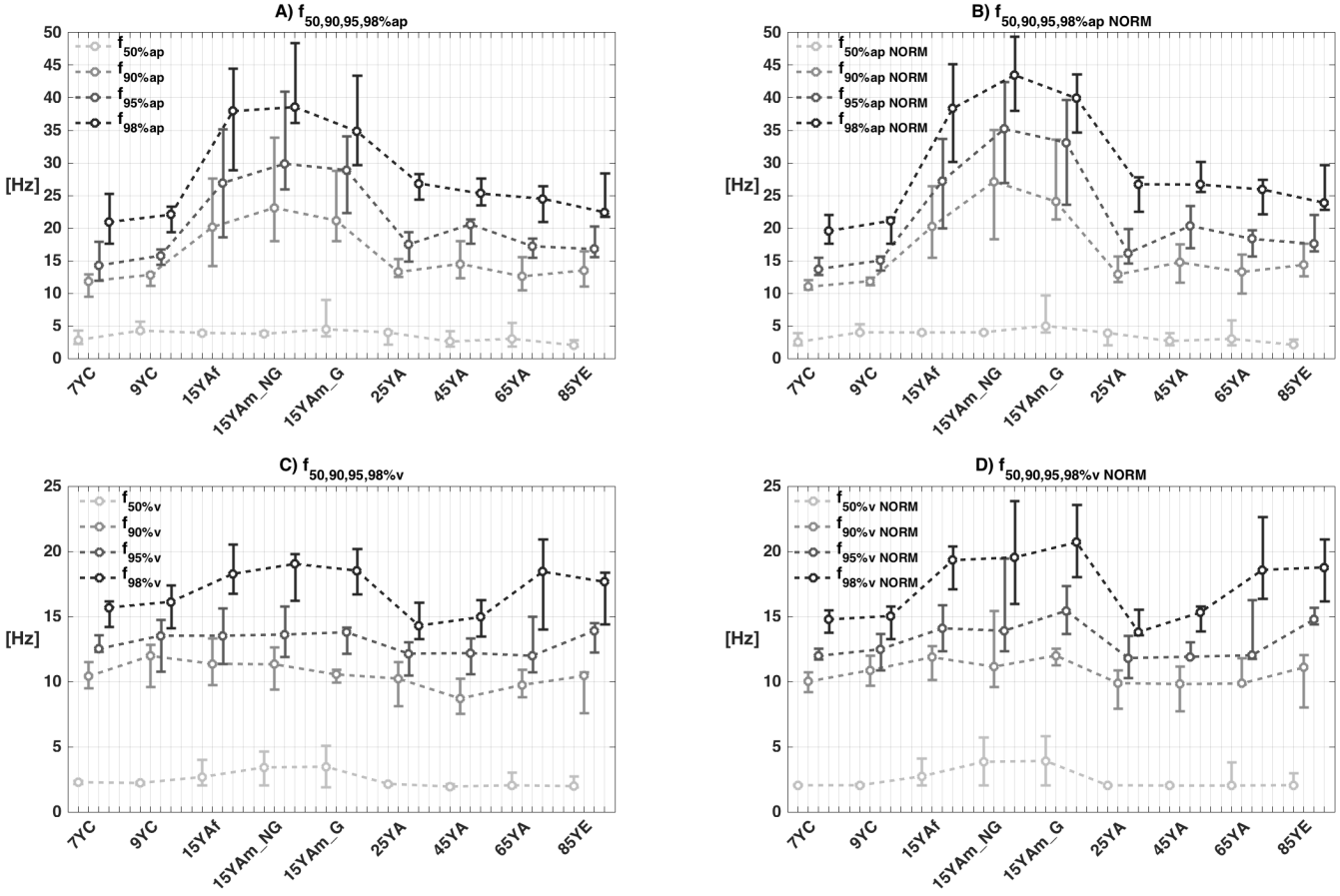

Figure 2: Median, 25- and 75-percentile of $f_{50,90,95,98\%}$ (A and C panels), and $f_{50,90,95,98\%_{NORM}}$ (B and D panels) on AP and ML direction respectively. Darkening grey tones are associated with increasing percentage of normalized power.

2.5 DISCUSSION

Accelerometric measures during gait are extensively used to evaluate motor function in both healthy (e.g. children, adolescents, adults, elderly) and pathological (e.g. Parkinson, Stroke) subjects [1–5]. In particular, trunk acceleration during gait allows assessing different characteristics of the motor pattern itself in different populations, from timing to more complex aspects of motor control, such as variability, stability, complexity and regularity, quantified by means of different indexes and metrics that, directly or indirectly, analyse the harmonic content of the signal.

However, spectrum of trunk acceleration during gait was not previously characterized in the literature, making even more critical the lack of standardization (e.g. sampling frequency, time duration of the signal) in signal acquisition and processing.

Therefore the fundamental frequency and the frequency corresponding to the 50, 90, 95 and 98% of the normalized power of the trunk acceleration during gait of nine age groups from 7 to 85 year-old were analysed.

For the purpose of the analysis, stationary of the analysed signal was verified [38,39] for durations of at least 20 seconds including an integer number of strides.

For a correct and reliable spectral analysis of a discrete, periodic and finite duration signals, two aspects have to be taken into account: the frequency resolution and the coherent sampling, both of them directly dependent on the signal windowing, thus, on the time duration of the signal itself.

The frequency resolution, that means the capacity to discriminate two near frequency components in the spectrum, is closely related to the duration of the analysed signal. Indeed, in the time domain, a finite length signal is a product between the signal, ideally of unlimited duration, and the window signal (usually a *rect* signal); this product becomes, in the frequency domain, a convolution product between the Fourier Transform of the analysed signal and of the window

signal (usually *sinc* one). The spectrum frequency resolution depends to the size of the main lobe of the window signal Fourier Transform (*sinc* signal). It follows that the obtained spectrum frequency resolution is proportional to the inverse of the time duration of the analysed signal; the proportionality factor is related to the used window signal [37]. The coherent sampling, when sampling frequency and the signal fundamental frequency are synchronized, is necessary to avoid spectral leakage, presence of unreal components in the spectrum. When the fundamental frequency of the signal is not a priori known, it is well practice to analyse signals including an integer number of periods (i.e. here strides) and/or to use a window signal able to reduce this effect [37]. The bias introduced by an inappropriate frequency resolution and/or incorrect coherent sampling could be limited both through an *ad-hoc* windowing and tuning the time duration of the signal [37]. Due to the absence, to the authors' knowledge, of literature about how different window signals could modify frequency analysis of trunk acceleration during gait and being the use of *rect* signal a *de facto* standard to windowing trunk acceleration, the authors' choice was to follow this same approach to allow comparison with other studies. In addition, the signal length of a minimum of 20 seconds was chosen to guarantee the minimum resolution frequency and an integer number of strides to avoid spectrum leakage. For this work a resolution frequency of at least 0.05 Hz -three orders of magnitude smaller than the highest possible frequency ($f_s/2 = 64$ Hz)- was used.

The obtained FF values are in agreement with the results of other studies [28,42,43], that analysed stride frequency (cadence), suggesting that the fundamental frequency (FF) corresponds to the stride frequency (cadence). Nevertheless, computing stride frequency directly from the signal spectrum and not in the time domain, as the inverse of mean stride time, is more robust to both errors resulting from stride detection and from outlier values, resulting from irregular isolated strides. Accordingly, the calculation of FF from the signal spectrum could be used as robust and reliable method to estimate reference cadence. Indeed, on the data of this study, differences in stride frequency, calculated in the time domain and directly from the signal spectrum, are in the range of 0.05-0.1 Hz. Even if these discrepancies could appear negligible, when

stride frequency is used to compute non-linear metrics for the gait assessment [13,14] can lead to incorrect results.

For groups 7YC, 9YC, 15YAf, 15YAm_NG, similar FF_{NORM} values were found, suggesting that in these groups stride frequency changes are more related to anthropometric characteristics [43,44] than to changes in motor control.

On the other hand, different FF_{NORM} values were observed in all other populations. In particular, 15YAm_G showed lower values than all other populations and than not grown peers (15YAf and 15YAm_NG), suggesting some relevant change in motor control in the adolescents dealing with a growth spurt [36]. Then, decreasing FF_{NORM} values were observed with age from 25YA to 85YA, suggesting an influence of aging [45,46].

The normalization of $f_{50,90,95,98\%_{ap,ml,v}}$ with respect to the FF was performed in order to evaluate if the fundamental frequency of each population influenced the harmonic content of the signal. The results showed similar values and trends, for normalized and non-normalized features, suggesting that the observed differences are peculiar of the populations.

Values of $f_{50,90,95,98\%}$ highlight how the spectrum, in AP and V direction, is characterized by a peak at low frequency (around 3.5 Hz) and then by a uniform and low power band, wider in AP than in V direction. ML direction, instead, is characterized by a flat spectrum.

In general, the results of the present study suggest operative indications about how the trunk acceleration signal should be acquired and processed: (i) if the harmonic content is directly analysed, not less than 20 seconds of duration with an integer number of strides should be analysed, allowing a sufficient frequency resolution and avoiding spectrum leakage; (ii) to ensure 98% of the harmonic content of the signal, a sampling frequency higher than 90 Hz for adolescents and higher than 60 Hz for the other age population should be used.

The limited number of subjects included for each population could be considered a limitation of the present study. On the other hand, the fact that gait is a motor paradigm and the limited dispersion of data in each population supports the results of the analysis. On the other hand, the obtained inferential statistics

results confirmed that the chosen age samples were representative of the corresponding populations. Moreover, even though, to the knowledge of the authors, frequency features of lower trunk acceleration signal during gait was not previously assessed in literature, therefore no specific comparison is possible, the results of the present work are in agreement with other studies [11,28,35,36,47,48] that indirectly analysing the harmonic content of trunk acceleration signal and stride frequency as related to age. The lack in the literature of similar studies given, this work is a preliminary study for more detailed analyses, eventually referring to different sites of acceleration measurement and/or different populations (i.e. pathologic populations), to which the present results can not be generalized.

Concluding, the present work provides a characterization of the spectrum of lower trunk acceleration signal during gait pattern as related to age in different populations, providing, for the first time, reference values for the proper signal acquisition and processing.

The calculation of fundamental frequency (FF) from trunk acceleration spectrum of a signal of sufficient duration can serve as a more robust approach for the estimation of mean cadence during gait.

The harmonic content (at 98%) of the acceleration signal for all the analysed population, with exception of the adolescents, is below 30 Hz where the high frequencies contribution is due to AP direction. On the other hand, the spectrum resulted to wide up to 45Hz when analysing adolescent populations.

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2.7 SUPPLEMENTARY MATERIAL

2.7.1 FF and FF_{NORM}

POPULATION	***FF*** [Hz]
	$\boldsymbol{FF_{NORM}}$ [-]
7YC	1.10 (1.05-1.15)
	0.30 (0.28-0.30)
9YC	1.08 (1.00-1.08)
	0.30 (0.29-0.31)
15YAf	0.98 (0.95-1.03)
	0.30 (0.29-0.30)
15YAm_NG	0.96 (0.93-1.03)
	0.30 (0.29-0.32)
15YAm_G	0.90 (0.85-0.93)
	0.28 (0.27-0.29)
25YA	1.03 (1.00-1.05)
	0.32 (0.30-0.31)
45YA	1.00 (0.91-1.05)
	0.31 (0.29-0.31)
65YA	0.95 (0.90-1.00)
	0.29 (0.27-0.31)
85YE	0.92 (0.88-0.95)
	0.28 (0.26-0.29)

Table 1: Median, 25- and 75-percentile of *FF* (white background), and FF_{NORM} (grey background).

2.7.2 $f_{50,90,95,98\%_{ap}}$

POPULATION	$f_{50\%_{ap}}$ [Hz]	$f_{90\%_{ap}}$ [Hz]	$f_{95\%_{ap}}$ [Hz]	$f_{98\%_{ap}}$ [Hz]
	$f_{50\%_{ap_{NORM}}}$ [-]	$f_{90\%_{ap_{NORM}}}$ [-]	$f_{95\%_{ap_{NORM}}}$ [-]	$f_{98\%_{ap_{NORM}}}$ [-]
7YC	2.80 (2.25-4.55)	12.23 (10.35-13.50)	15.08 (12.35-18.20)	22.08 (18.25-25.6)
	2.47 (2.05-3.96)	11.03 (10.71-12.56)	14.02 (12.77-15.49)	20.60 (17.74-23.19)
9YC	4.30 (4.15-5.50)	12.60 (10.85-13.10)	15.55 (14.25-16.80)	21.87 (19.35-23.30)
	4.05 (4.00-5.12)	11.79 (10.85-12.41)	14.88 (13.26-15.60)	20.40 (17.59-21.67)
15YAf	3.90 (3.75-5.70)	20.30 (14.25-26.60)	26.30 (19.85-34.25)	37.63 (31.50-44.55)
	3.98 (3.71-5.85)	21.59 (13.90-25.33)	28.09 (19.33-32.62)	39.10 (30.73-45.69)
15YAm_NG	3.78 (3.55-4.10)	23.00 (17.90-34.20)	29.85 (25.60-41.40)	37.85 (36.00-48.45)
	4.05 (4.00-4.06)	22.64 (16.78-35.08)	29.35 (22.09-42.46)	39.29 (35.22-50.44)
15YAm_G	3.70 (3.45-9.45)	24.38 (18.95-29.18)	32.05 (22.40-34.70)	35.90 (33.00-43.45)
	4.05 (3.94-9.65)	26.90 (21.37-33.26)	36.52 (23.58-39.80)	41.62 (35.68-43.75)
25YA	2.63 (2.15-4.10)	13.38 (12.25-14.05)	16.43 (15.30-19.15)	24.70 (22.30-27.35)
	2.48 (2.05-4.00)	13.06 (11.36-13.71)	15.83 (14.23-17.50)	23.53 (21.24-26.68)
45YA	2.625 (1.85-4.20)	14.65 (12.40-18.10)	20.85 (17.75-21.40)	25.55 (23.90-27.75)
	2.71 (2.15-3.89)	15.11 (11.81-17.66)	20.69 (17.07-23.54)	27.02 (25.53-30.00)
65YA	2.13 (1.95-4.20)	12.35 (10.45-15.50)	17.70 (15.60-20.40)	24.55 (20.80-27.70)
	2.16 (2.10-4.00)	13.15 (9.95-16.32)	18.88 (15.60-23.31)	25.32 (22.26-29.26)
85YE	1.98 (1.85-2.70)	12.80 (10.80-15.60)	16.85 (14.70-18.25)	22.15 (20.25-23.90)
	2.08 (2.05-2.92)	14.08 (12.00-17.49)	17.52 (16.21-22.12)	24.06 (21.89-28.97)

Table 2: Median, 25- and 75-percentile of $f_{50,90,95,98\%}$ (white background), and $f_{50,90,95,98\%_{NORM}}$ (grey background) in AP direction.

2.7.3 $f_{50,90,95,98\%_{ml}}$

POPULATION	$f_{50\%_{ml}}$ [Hz]	$f_{90\%_{ml}}$ [Hz]	$f_{95\%_{ml}}$ [Hz]	$f_{98\%_{ml}}$ [Hz]
	$f_{50\%_{ml_{NORM}}}$ [-]	$f_{90\%_{ml_{NORM}}}$ [-]	$f_{95\%_{ml_{NORM}}}$ [-]	$f_{98\%_{ml_{NORM}}}$ [-]
7YC	7.35 (7.10-8.10)	11.97 (11.45-13.05)	14.15 (13.15-14.8)	17.78 (15.75-18.85)
	6.92 (6.45-8.71)	11.07 (10.57-12.05)	12.82 (12.52-13.59)	15.91 (15.30-18.06)
9YC	8.38 (7.30-9.20)	12.20 (11.5-13.25)	14.05 (13.15-14.85)	17.10 (16.05-18.25)
	7.81 (6.91-8.36)	11.22 (10.80-12.55)	13.07 (12.81-14.32)	15.98 (15.52-17.45)
15YAf	6.80 (6.35-7.15)	13.22 (11.85-14.45)	16.05 (14.35-16.95)	19.75 (16.60-21.25)
	6.90 (6.80-7.06)	13.48 (11.85-14.82)	15.76 (14.72-17.72)	19.62 (17.03-22.36)
15YAm_NG	6.80 (5.70-7.05)	13.10 (11.20-14.50)	16.35 (13.8-17.25)	19.05 (18.05-20.90)
	6.97 (5.84-8.00)	14.99 (10.93-15.26)	18.18 (13.09-18.62)	21.57 (17.11-22.67)
15YAm_G	6.90 (6.05-8.30)	12.08 (11.25-14.45)	14.23 (13.15-17.65)	19.25 (16.85-22.80)
	7.29 (6.90-9.06)	14.21 (12.50-16.23)	16.81 (14.94-18.30)	22.66 (18.39-24.19)
25YA	5.38 (3.30-7.45)	11.05 (10.25-12.55)	14.20 (12.00-16.10)	17.40 (15.40-18.65)
	5.73 (3.07-6.93)	11.04 (9.86-12.73)	14.57 (11.95-15.33)	16.86 (15.95-18.52)
45YA	4.95 (4.25-5.85)	10.13 (9.45-12.15)	13.18 (11.40-17.10)	17.53 (15.35-20.95)
	4.95 (4.05-6.83)	11.33 (9.00-12.97)	14.25 (10.97-16.68)	18.19 (16.81-21.49)
65YA	6.30 (5.25-8.25)	10.98 (10.10-13.45)	14.80 (12.25-17.05)	19.68 (18.45-21.85)
	6.91 (5.14-8.68)	11.73 (11.10-14.94)	15.19 (13.29-18.94)	21.59 (18.29-23.78)
85YE	6.35 (4.35-7.35)	11.65 (10.20-14.65)	13.08 (12.15-17.80)	16.30 (14.60-23.45)
	7.12 (4.95-7.74)	14.12(11.33-15.80)	15.85(13.50-18.85)	18.65(16.61-24.47)

Table 3: Median, 25- and 75-percentile of $f_{50,90,95,98\%}$ (white background), and $f_{50,90,95,98\%_{NORM}}$ (grey background) in ML direction.

2.7.4 $f_{50,90,95,98\%_v}$

POPULATION	$f_{50\%_v}$ [Hz]	$f_{90\%_v}$ [Hz]	$f_{95\%_v}$ [Hz]	$f_{98\%_v}$ [Hz]
	$f_{50\%_{v_{NORM}}}$ [-]	$f_{90\%_{v_{NORM}}}$ [-]	$f_{95\%_{v_{NORM}}}$ [-]	$f_{98\%_{v_{NORM}}}$ [-]
7YC	2.33 (2.20-2.45)	10.65 (8.90-11.70)	12.88 (12.15-13.60)	15.63 (14.35-16.15)
	2.07 (2.05-2.09)	10.00 (9.86-10.68)	11.98 (11.76-12.36)	14.49 (14.00-14.95)
9YC	2.23 (2.20-2.45)	12.05 (9.70-12.90)	13.63 (11.19-14.75)	16.15 (14.25-17.69)
	2.09 (2.05-2.28)	10.95 (9.70-12.00)	12.52 (11.10-13.72)	15.02 (13.62-16.00)
15YAf	2.93 (2.10-4.25)	11.30 (9.80-12.05)	13.48 (11.40-14.90)	18.53 (16.65-20.45)
	2.84 (2.10-4.72)	11.88 (10.05-12.76)	14.00 (11.69-16.26)	18.64 (17.08-21.69)
15YAm_NG	3.55 (2.10-4.70)	11.20 (9.40-12.75)	13.93 (12.00-15.80)	19.28 (16.80-20.60)
	3.02 (2.05-5.84)	10.87 (9.84-15.21)	14.09 (12.31-19.75)	19.56 (17.59-24.31)
15YAm_G	4.15 (3.10-5.15)	10.95 (10.20-12.10)	13.85 (12.15-15.25)	17.65 (16.90-20.25)
	4.49 (3.88-5.83)	12.19 (11.58-13.44)	15.39 (13.89-17.53)	19.36 (18.16-23.58)
25YA	2.15 (2.10-2.20)	9.80 (8.20-10.55)	11.48 (10.15-12.80)	14.18 (12.80-14.55)
	2.05 (2.05-2.10)	9.97 (7.90-10.20)	11.86 (9.90-12.85)	13.86 (13.07-15.52)
45YA	1.98 (1.80-2.15)	8.68 (7.60-10.30)	12.35 (10.60-13.35)	15.03 (13.60-16.60)
	2.05 (2.05-2.06)	9.86 (7.81-11.38)	12.06 (11.87-12.53)	15.62 (14.06-16.00)
65YA	2.15 (1.95-3.10)	9.58 (8.80-10.55)	12.18 (10.60-13.95)	17.55 (13.90-21.75)
	2.06 (2.05-3.94)	10.05 (9.57-10.57)	12.77 (11.55-13.67)	18.29 (16.90-22.89)
85YE	2.05 (1.90-2.40)	10.03 (8.35-11.05)	14.18 (12.40-14.65)	18.18 (14.15-19.20)
	2.06 (2.05-2.74)	10.45 (9.03-13.39)	15.19 (13.74-15.72)	19.28 (17.15-20.72)

Table 4: Median, 25- and 75-percentile of $f_{50,90,95,98\%}$ (white background), and $f_{50,90,95,98\%_{NORM}}$ (grey background) in V direction.

2.8 REFERENCES

[1] A.I. Cuesta-Vargas, A. Galán-Mercant, J.M. Williams, The use of inertial sensors system for human motion analysis, Phys. Ther. Rev. 15 (2010) 462–473. doi:10.1179/1743288X11Y.0000000006.

[2] A. Dalton, H. Khalil, M. Busse, A. Rosser, R. van Deursen, G. ÓLaighin, Analysis of gait and balance through a single triaxial accelerometer in presymptomatic and symptomatic Huntington's disease, Gait Posture. 37 (2013) 49–54. doi:10.1016/j.gaitpost.2012.05.028.

[3] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration Patterns of the Head and Pelvis When Walking Are Associated With Risk of Falling in Community-Dwelling Older People, J. Gerontol. A. Biol. Sci. Med. Sci. 58 (2003) M446–M452. doi:10.1093/gerona/58.5.M446.

[4] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Age-related differences in walking stability, Age Ageing. 32 (2003) 137–142. doi:10.1093/ageing/32.2.137.

[5] P. Fazio, G. Granieri, I. Casetta, E. Cesnik, S. Mazzacane, P. Caliandro, F. Pedrielli, E. Granieri, Gait measures with a triaxial accelerometer among patients with neurological impairment, Neurol. Sci. 34 (2013) 435–440. doi:10.1007/s10072-012-1017-x.

[6] GAIT ANALYSIS - PERRY J. / BURNFIELD J.M. - Slack Incorporated - Ortopedia :, Libr. Cortina Milano. (n.d.). https://www.libreriacortinamilano.it/medicina/terapia-fisica-e-riabilitazione/riabilitazione-motoria/9781556427664/gait-analysis.html?fc=controller (accessed July 28, 2017).

[7] W. Zijlstra, A.L. Hof, Assessment of spatio-temporal gait parameters from trunk accelerations during human walking, Gait Posture. 18 (2003) 1–10. doi:10.1016/S0966-6362(02)00190-X.

[8] W. Zijlstra, Assessment of spatio-temporal parameters during unconstrained walking, Eur. J. Appl. Physiol. 92 (2004) 39–44. doi:10.1007/s00421-004-1041-5.

[9] A. Ferrari, L. Chiari, P. Ginis, L. Rocchi, Step length estimation using shoe-mounted inertial sensors: Application in clinical settings, Gait Posture. 39 (2014) S47. doi:10.1016/j.gaitpost.2014.04.066.

[10] F. Riva, M.C. Bisi, R. Stagni, Gait variability and stability measures: Minimum number of strides and within-session reliability, Comput. Biol. Med. 50 (2014) 9–13. doi:10.1016/j.compbiomed.2014.04.001.

[11] M.C. Bisi, F. Riva, R. Stagni, Measures of gait stability: performance on adults and toddlers at the beginning of independent walking, J. NeuroEngineering Rehabil. 11 (2014). doi:10.1186/1743-0003-11-131.

[12] D. Hamacher, D. Hamacher, A. Törpel, M. Krowicki, F. Herold, L. Schega, The reliability of local dynamic stability in walking while texting and performing an arithmetical problem, Gait Posture. 44 (2016) 200–203. doi:10.1016/j.gaitpost.2015.12.021.

[13] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration patterns of the head and pelvis when walking on level and irregular surfaces, Gait Posture. 18 (2003) 35–46. doi:10.1016/S0966-6362(02)00159-5.

[14] C.J.C. Lamoth, P.J. Beek, O.G. Meijer, Pelvis–thorax coordination in the transverse plane during gait, Gait Posture. 16 (2002) 101–114. doi:10.1016/S0966-6362(01)00146-1.

[15] M. Costa, C.-K. Peng, A. L. Goldberger, J.M. Hausdorff, Multiscale entropy analysis of human gait dynamics, Phys. Stat. Mech. Its Appl. 330 (2003) 53–60. doi:10.1016/j.physa.2003.08.022.

[16] N.M. Kosse, S. Caljouw, D. Vervoort, N. Vuillerme, C.J.C. Lamoth, Validity and Reliability of Gait and Postural Control Analysis Using the Tri-axial Accelerometer of the iPod Touch, Ann. Biomed. Eng. 43 (2015) 1935–1946. doi:10.1007/s10439-014-1232-0.

[17] T. Isho, H. Tashiro, S. Usuda, Accelerometry-Based Gait Characteristics Evaluated Using a Smartphone and Their Association with Fall Risk in People with Chronic Stroke, J. Stroke Cerebrovasc. Dis. 24 (2015) 1305–1311. doi:10.1016/j.jstrokecerebrovasdis.2015.02.004.

[18] R.J. Ellis, Y.S. Ng, S. Zhu, D.M. Tan, B. Anderson, G. Schlaug, Y. Wang, A Validated Smartphone-Based Assessment of Gait and Gait Variability in Parkinson's Disease, PLoS ONE. 10 (2015). doi:10.1371/journal.pone.0141694.
[19] A. Hartmann, K. Murer, R.A. de Bie, E.D. de Bruin, Reproducibility of spatio-temporal gait parameters under different conditions in older adults using a trunk tri-axial accelerometer system, Gait Posture. 30 (2009) 351–355. doi:10.1016/j.gaitpost.2009.06.008.
[20] N.M. Kosse, N. Vuillerme, T. Hortobágyi, C.J. Lamoth, Multiple gait parameters derived from iPod accelerometry predict age-related gait changes, Gait Posture. 46 (2016) 112–117. doi:10.1016/j.gaitpost.2016.02.022.
[21] M. Mancini, A. Salarian, P. Carlson-Kuhta, C. Zampieri, L. King, L. Chiari, F.B. Horak, ISway: a sensitive, valid and reliable measure of postural control, J. NeuroEngineering Rehabil. 9 (2012) 59. doi:10.1186/1743-0003-9-59.
[22] M. El-Gohary, S. Pearson, J. McNames, M. Mancini, F. Horak, S. Mellone, L. Chiari, Continuous Monitoring of Turning in Patients with Movement Disability, Sensors. 14 (2013) 356–369. doi:10.3390/s140100356.
[23] J.M. Huisinga, M. Mancini, R. St. George, F. Horak, Accelerometry reveals differences in gait variability between patients with multiple sclerosis and healthy controls, Ann. Biomed. Eng. 41 (2013) 1670–1679. doi:10.1007/s10439-012-0697-y.
[24] E. Sejdic, K.A. Lowry, J. Bellanca, M.S. Redfern, J.S. Brach, A Comprehensive Assessment of Gait Accelerometry Signals in Time, Frequency and Time-Frequency Domains, IEEE Trans. Neural Syst. Rehabil. Eng. 22 (2014) 603–612. doi:10.1109/TNSRE.2013.2265887.
[25] M.N. Nyan, F.E.H. Tay, K.H.W. Seah, Y.Y. Sitoh, Classification of gait patterns in the time–frequency domain, J. Biomech. 39 (2006) 2647–2656. doi:10.1016/j.jbiomech.2005.08.014.
[26] C. Angeloni, P.O. Riley, D.E. Krebs, Frequency content of whole body gait kinematic data, IEEE Trans. Rehabil. Eng. 2 (1994) 40–46. doi:10.1109/86.296343.
[27] D.C. James, K.N. Mileva, D.P. Cook, Low-frequency accelerations over-estimate impact-related shock during walking, J. Electromyogr. Kinesiol. 24 (2014) 264–270. doi:10.1016/j.jelekin.2013.12.008.
[28] F. Danion, E. Varraine, M. Bonnard, J. Pailhous, Stride variability in human gait: the effect of stride frequency and stride length, Gait Posture. 18 (2003) 69–77. doi:10.1016/S0966-6362(03)00030-4.
[29] W. Zijlstra, A.L. Hof, Displacement of the pelvis during human walking: experimental data and model predictions, Gait Posture. 6 (1997) 249–262. doi:10.1016/S0966-6362(97)00021-0.
[30] J. McCamley, M. Donati, E. Grimpampi, C. Mazzà, An enhanced estimate of initial contact and final contact instants of time using lower trunk inertial sensor data, Gait Posture. 36 (2012) 316–318. doi:10.1016/j.gaitpost.2012.02.019.
[31] K. Aminian, B. Najafi, C. Büla, P.-F. Leyvraz, P. Robert, Spatio-temporal parameters of gait measured by an ambulatory system using miniature gyroscopes, J. Biomech. 35 (2002) 689–699. doi:10.1016/S0021-9290(02)00008-8.
[32] D. Hamacher, D. Hamacher, N.B. Singh, W.R. Taylor, L. Schega, Towards the assessment of local dynamic stability of level-grounded walking in an older population, Med. Eng. Phys. 37 (2015) 1152–1155. doi:10.1016/j.medengphy.2015.09.007.
[33] E.A.F. Ihlen, A. Weiss, A. Bourke, J.L. Helbostad, J.M. Hausdorff, The complexity of daily life walking in older adult community-dwelling fallers and non-fallers, J. Biomech. 49 (2016) 1420–1428. doi:10.1016/j.jbiomech.2016.02.055.
[34] P. Tamburini, D. Mazzoli, R. Stagni, Towards an objective assessment of motor function in sub-acute stroke patients: Relationship between clinical rating scales and instrumental gait stability indexes, Gait Posture. 59 (2018) 58–64. doi:10.1016/j.gaitpost.2017.09.033.
[35] M.C. Bisi, R. Stagni, Complexity of human gait pattern at different ages assessed using multiscale entropy: From development to decline, Gait Posture. 47 (2016) 37–42. doi:10.1016/j.gaitpost.2016.04.001.
[36] M.C. Bisi, R. Stagni, Development of gait motor control: what happens after a sudden increase in height during adolescence?, Biomed. Eng. OnLine. 15 (2016). doi:10.1186/s12938-016-0159-0.
[37] V. Madisetti, Digital Signal Processing Fundamentals, CRC Press, 2009.

[38] Random Data: Analysis and Measurement Procedures, 4th Edition - Julius S. Bendat, Allan G. Piersol, (n.d.). http://www.wiley.com/WileyCDA/WileyTitle/productCd-0470248777.html (accessed July 31, 2017).
[39] G. Enderlein, Nonparametric Methods for Quantitative Analysis. American Sciences Press Inc., Columbus/Ohio 1976, Biom. J. 27 (1985) 490–490. doi:10.1002/bimj.4710270503.
[40] A.L. Hof, Scaling gait data to body size, Gait Posture. 4 (1996) 222–223. doi:10.1016/0966-6362(95)01057-2.
[41] C.M. Jarque, A.K. Bera, A Test for Normality of Observations and Regression Residuals, Int. Stat. Rev. Rev. Int. Stat. 55 (1987) 163. doi:10.2307/1403192.
[42] R.J. Beck, T.P. Andriacchi, K.N. Kuo, R.W. Fermier, J.O. Galante, Changes in the gait patterns of growing children., J Bone Jt. Surg Am. 63 (1981) 1452–1457.
[43] D.H. Sutherland, R. Olshen, L. Cooper, S.L. Woo, The development of mature gait., J Bone Jt. Surg Am. 62 (1980) 336–353.
[44] Gait Analysis: Normal and Pathological Function, J. Sports Sci. Med. 9 (2010) 353.
[45] Y. Barak, R.C. Wagenaar, K.G. Holt, Gait Characteristics of Elderly People With a History of Falls: A Dynamic Approach, Phys. Ther. 86 (2006) 1501–1510. doi:10.2522/ptj.20050387.
[46] B.E. Maki, Gait Changes in Older Adults: Predictors of Falls or Indicators of Fear?, J. Am. Geriatr. Soc. 45 (1997) 313–320. doi:10.1111/j.1532-5415.1997.tb00946.x.
[47] F. Riva, M.J.P. Toebes, M. Pijnappels, R. Stagni, J.H. van Dieën, Estimating fall risk with inertial sensors using gait stability measures that do not require step detection, Gait Posture. 38 (2013) 170–174. doi:10.1016/j.gaitpost.2013.05.002.
[48] K.A. Lowry, N. Lokenvitz, A.L. Smiley-Oyen, Age- and speed-related differences in harmonic ratios during walking, Gait Posture. 35 (2012) 272–276. doi:10.1016/j.gaitpost.2011.09.019.

Chapter 3

CONTINUOS MONITORING: FROM LABORATORY TO PORTABLE DEVICE, INFLUENCE OF SAMPLING FREQUENCY

Some say they see poetry in my paintings;
I see only science.
Georges Seurat

Sampling is kind of prehistoric,
given the technology and the textures you can create.
Macklemore

[1]To Submit to IEEE Transactions on Biomedical Engineering. *Fall risk monitoring: from laboratory to portable device, influence of sampling frequency*. Tamburini P, Stagni R.

3. CONTINUOS MONITORING: FROM LABORATORY TO PORTABLE DEVICE, INFLUENCE OF SAMPLING FREQUENCY

3.1 ABSTRACT

The understanding of locomotor stability is a critical issue in the assessment of fall risk in both pathological and elderly subjects. Clinical assessment of fall risk is typically based on clinical rating scales that heavily rely on the clinician's subjective judgment. Instrumental stability and variability indexes of gait can represent a promising solution for the objective quantification of locomotor functionality and fall risk. Furthermore, stability and variability indexes have shown promising correlations with clinical scales, potentially providing a better insight in the functional analysis of gait pattern.

For an effective exploitation of this approach, the subject's gait can be analysed in daily living conditions, acquiring a large number of strides to guarantee acceptable measure reliability. This is possible with a continuous monitoring of subjects at risk. A smartphone can be the ideal device for this goal, since it is user friendly and cheap. On the other hand, although the inertial measurement units mounted on it have nothing to envy to other commercially available devices, the sampling frequency at 100-200 Hz is not compatible with the multiple functions performed by a conventional device. Thus, the influence of reduced (from 128 to 42.6 Hz) sampling frequency on the estimated variability and stability indexes was investigated. The results highlight that down-sampling (at 42.6 Hz) is viable, if specific constraints are taken into account in the implementation of the analysed metrics.

Key words: *fall risk; fall risk assessment; fall risk monitoring; under-sampling gait acceleration; elderly; stability and variability indexes.*

3.2 INTRODUCTION

ABBREVIATIONS

ORG	Acquired signal
FILT	Filtered signal
UNDER	Under-sampled signal
INTERP	Interpolated signal
SD	Standard Deviation
CV	Coefficient of Variation
NI	Non-stationary Index
IV	Inconsistency of the variance
PSD1	Short term variability of stride estimated *via* Poincaré plots
PSD2	Long term variability of stride estimated *via* Poincaré plots
HR	Harmonic Ratio
IH	Index of Harmonicity
sLE	Short term Lyapunov Exponent
lLE	Long term Lyapunov Exponent on the vertical acceleration direction
RQA	Recurrence Quantification Analysis
rr	Recurrence Rate
Det	Determinism
AvgL	Averaged diagonal line length
SEN	Sample entropy

The understanding and assessment of gait stability is a fundamental step to identify the subject's risk of falling, since falls often occur during walking among older adults [1]. Subject specific factors leading to fall risk should be identify in order to perform effective clinical intervention.

Recent studies [2,3] demonstrated that clustering appropriate selected indexes provides indication regarding the specific subject alterations increasing fall risk. Even though promising results were shown, several variability and stability indexes require a high number of strides in order to guarantee an acceptable reliability [4] of the measure.

The effective exploitation of this approach is meant in its implementation on a portable device for the continuous monitoring of subjects at risk. This would allow the acquisition of a large number of strides, as well as the continuous monitoring of motor stability in daily living conditions. The ideal device to maximize the exploitation together with subject's acceptance can be a smart device, such as a modern smartphone.

The accelerometers, in general the inertial measurement units (IMUs), embedded in modern smartphones, have nothing to envy to other commercially available devices used mainly for research purpose. Several studies [5–8] have demonstrated that smartphone accelerometers display similar performance in terms of accuracy, although they do not guarantee sampling frequencies comparable with those conventionally adopted [9], due to the provided multiple functions and required memory storage.

On one hand, the non-constant sampling could be compensated using interpolation techniques of variable complexity [9–11]; on the other hand, the influence of a reduced sampling frequency, usually at 50 Hz for Android systems [9], could not be *a priori* evaluated or neglected, considering also the non linear nature of the analysed variability and stability indexes.

This analysis is an essential step to transfer gait assessment from the laboratory to the real practice without loosing relevant information. Despite its importance, to the knowledge of the authors, this specific aspect was not assessed previously in the literature.

From signal theory, it is known that the down-sampling process has, in general, two effects on the signal: one in the time domain, due to the reduction of the number of samples (i.e. sample effect), and one in the frequency domain, (i.e. frequency effect) associated with the aliasing occurring, as all the frequency components above the half of the new sampling frequency (under-sampling Nyquist frequency) are not zero, accordingly to Shannon theorem.

Mathematically, the sample effect can be compensated using an interpolation algorithm that does not include new (i.e. high) frequency components, using interpolation as an artifice to just increase the number of samples without changing the frequency content of the signal. On the other hand, no compensation is possible for frequency effect.

The aim of the present study was to evaluate the influence of a reduced sampling frequency in the computation of stability and variability indexes, used for the assessment of gait in young healthy subjects.

3.3 MATERIALS and METHODS

3.3.1 Participants

Sixteen healthy young subjects (24 ± 2 year, 65.3 ± 13 kg, 169 ± 10 cm, 5 males e 11 females) were enrolled in the study. Only subjects with no self-reported history of locomotor disturbances or injuries that could affect their normal walking behaviour, or cause fatigue during the experimental protocol were included. The Review Board Committee of the authors' institution approved the study, and informed consent was obtained from all participants.

3.3.2 Experimental setup

The subjects performed a walking task outdoor in a quiet open space within the university premises, on a flat surface, along a straight path at self-selected speed on 250 m long dead-end road. During the task the participants did not have verbal interaction with other people, or other contact with obstacle causing possible distractions.

Subjects wore 2 tri-axial accelerometers (Opal, APDM, USA), one located at the level of the fifth lumbar vertebra, to acquire the trunk acceleration, and one on the right ankle needed for the stride detection [12].

Acceleration and angular velocity in vertical (V), medio-lateral (ML) and antero-posterior (AP) directions were acquired with a sampling frequency (f_s) at 128 Hz.

3.3.3 Signal Processing

In order to evaluate the influence of a reduced sampling frequency, three different signals, from the acquired trunk acceleration and ankle angular velocity (ORG), were calculated:

- filtered (FILT)
- under sampled (UNDER)
- interpolated (INTERP)

as schematically depicted in Figure 1.

Signal processing was implemented in Matlab 2015b (MathWorks BV, USA).

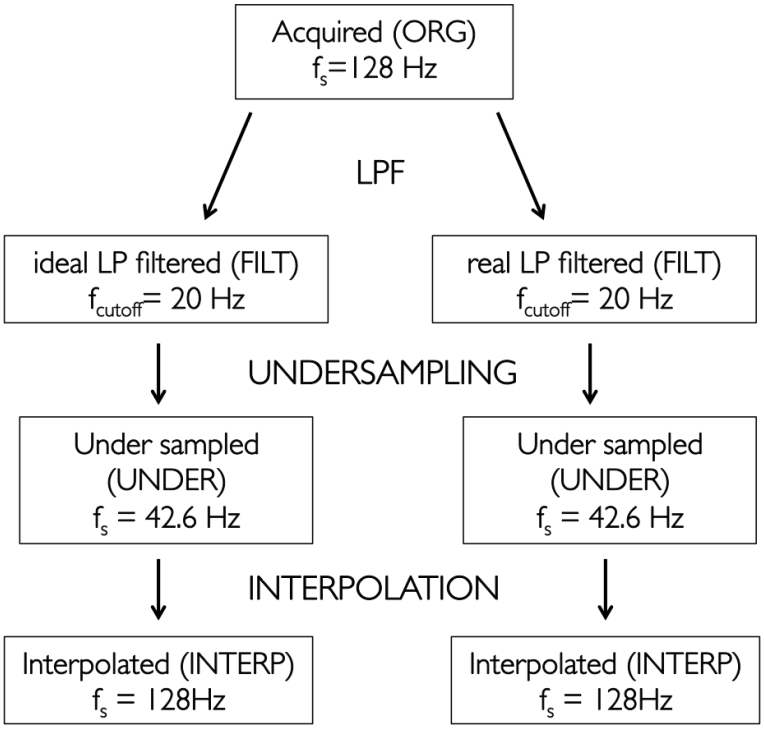

Figure 1: Flowchart of the performed signal processing.

Filtered Signal

The filtered signals were obtained using two different processing procedures: real and ideal low pass filtering with a cut off frequency at 20 Hz, in order to assess also the effect of a different filtering process.

The real low pass filter was obtained using MatLab 2015b built-in *Filter building application*, that given the desired filter characteristics (e.g. filter response, impulse response, pass band and stop band frequency, pass band ripple, and stop band attenuation) returned the filter coefficient and parameters. Thus, signals with different frequency content than the original one, but with same number of samples, were obtained.

The real filters characteristics are reported in Table 1.

REAL LOW PASS FILTER

FILTER SPECIFICATION		**ALGORITHM**	
Impulse response	F.I.R	Design Method	Equal ripple
Order filter	Minimum	Design Options	MatLab default
Filter type	Single Rate	**FILTER IMPLEMENTATION**	
FREQUNCY SPECIFICATION		Structure	Direct Form
Pass Band [-] ([Hz])	0.3125 (20 Hz)	**FEATURE**	
Stop Band [-] ([Hz])	0.3281 (21 Hz)	Phase Delay	198
MAGNITUDE SPECIFICATION		Phase Group Delay	198
Pass Band Ripple [dB]	1	ABS(FFT) in 21 Hz	0.37
Stop Band Attenuation [dB]	100	Re{FFT} in 21 Hz	-0,35

Table 1: Real low pass filters characteristics (MatLab built-in Toolbox).

Under-sampled Signal:

Once the original signals were filtered, an under-sampling process was performed. The under-sampling frequency (f_{s_UNDER}) was chosen three times smaller than the acquisition one (f_s = 128 Hz), obtaining a f_{s_UNDER} = 42.6 Hz lower than the smartphone allowed sampling frequency [9].

This way, a signal with equal frequency content of the filtered one, but with different number of samples (three times less), was obtained.

Interpolated Signal:

Once the original signals were filtered and under-sampled, an interpolation process, in order to obtain signals with a sampling frequency equal to the acquisition one but without frequency components above $f_{s\_UNDER}/2$, was performed. Thus, signals with same frequency content of the under-sampled one and with same number of samples of the original one was obtained.

3.3.4 Stability and Variability Indexes:

Stride detection was estimated from the angular velocity around the medio-lateral axis of the ankle [12] for each signal (i.e. original, filtered, under-sampled, and interpolated) and stride times were calculated accordingly. The first and last three strides were removed in order to exclude both gait initiation and termination phases, 200 strides were analysed in all the conditions.

The following variability indexes were calculated on the stride time series of each subject and signal (i.e. filtered, under-sampled, and interpolated):

Variability indexes:

- Standard deviation of the stride time (SD);
- Coefficient of Variation (CV) [13]
- Non-stationary Index (NI) [13]
- Inconsistency of the variance (IV) [13]
- Short and Long term variability of stride estimated *via* Poincaré plots (PSD1 and PSD2) [14].

For all the subjects and for each obtained trunk acceleration signal (i.e. filtered, under-sampled, and interpolated) the following stability indexes were performed:

Stability indexes:

- Harmonic Ratio (HR_v, HR_ap, HR_ml) [15] (see Chapter 1 for more details);
- Index of Harmonicity (IH_v, IH_ap, IH_ml) [15]
- Recurrence Quantification Analysis (RQA) implying the calculation of recurrence rate (RR), determinism (DET) and averaged diagonal line length (AvgL) [17] (see Chapter 1 for more details);
- Short term Lyapunov exponents (sLE_v, sLE_ap, sLE_ml) [16] (see Chapter 1 for more details);
- Sample entropy (SEN_v, SEN_ml and SEN_ap) [18] (see Chapter 1 for more details).

Indexes Parameters:

As detailed explained in Chapter 1, most of the indexes parameters depend on the sampling frequency, consequently their values were tuned accordingly (i.e. $f_{s\_UNDER} = f_s/3$). Moreover, all the parameters values were chosen following the indication reported in Chapter 1. In Table 2 all the used parameters values are shown:

INDEX	PARAMETERS	SIGNALS			
		ORG	FILT	UNDER	INTERP
SD	**Nr strides**	200	-	-	-
CV	**Nr strides**	200	-	-	-
NI	**Nr strides**	200	-	-	-
IV	**Nr strides**	200	-	-	-
PSD1	**Nr strides**	200	-	-	-
PSD2	**Nr strides**	200	-	-	-
RQA	**Nr strides**	200	-	-	-
	lag	10 samples	-	3 samples	-
	eD	5	-	-	-
	m	4	-	-	-
LE	**Nr strides**	200	-	-	-
	lag	10 samples	-	3 samples	-
	eD	5	-	-	-
SEN	**Nr strides**	200	-	-	-
	m	2	-	-	-
	r	0.2	-	-	-
	τ	3 and 6	-	1 and 2	-

Table 2: Indexes parameters. - indicates no change from the acquisition parameters (ORG column).

3.3.5 Statistical Analysis:

A Shapiro-Wilk test was performed on all the above-mentioned indexes, calculated for all the signals, showing that the data were not normally distributed. Kruskal-Wallis test with minimum level of significance (*p_value*) of 5% were performed to compare the indexes values obtained on the four different signals. If a significant interaction was found (*p_value* < 5%), Tukey-Kramer correction was considered for post-hoc analysis. In particular the multiple comparisons performed were:

1. Original signal *vs* filtered one, in order to evaluate the frequency effect.
2. Filtered signal *vs*, under-sampled one, in order to evaluate the sample effect.
3. Filtered signal *vs* interpolated one, in order to assess if an interpolation could solve the sample effect.
4. Original signal *vs* under-sampled one, to evaluate the overlapping of the sample and frequency effects.

As it concerns MSE, coarse-grained procedure with τ = 3 and 6 for the original signal (f_s = 128 Hz) were compared to coarse-grained procedure with τ = 1 and 2 for the under sampled ($f_{s\_UNDER} = f_s/3$ = 42.6 Hz) one.

3.4 RESULTS

Similar results were obtained using the signal filtered with an ideal low pass filter or a real one.

The statistical analysis results showed that all the variability (SD, CV, NI, IV, PSD1, and PSD2) indexes were not influenced by the under-sampling process.

Stability indexes displayed two different behaviours:

- No significant differences between stability indexes (HR, LE, and SEN in all the directions) calculated on the acquired signal and on the under sampled one, mining that these indexes were not influenced by the under-sampling process.
- Significant differences between stability indexes (det, AvgL, Max, and Div in all the directions) calculated on the filtered signal and on the under sampled one. However, concurrently, the same indexes showed no significant differences between the values obtained from the filtered signal and the interpolated one; mining that these indexes were influenced by the under-sampling process, suffering of the sample effect, however the interpolation process solved this problem making under-sampling eligible.

In Table 4 the obtained results were summarized.

	Frequency Effect	***Sample Effect***	***Interpolation Solved Sample Effect***	***Under-sampling Allowed***	***Under-sampling Allowed with Interpolation***
SD				✓	
CV				✓	
NI				✓	
IV				✓	

	Frequency Effect	*Sample Effect*	*Interpolation Solved Sample Effect*	*Under-sampling Allowed*	*Under-sampling Allowed with Interpolation*
PSD1				✓	
PSD2				✓	
HR_ap				✓	
HR_ml				✓	
HR_v				✓	
IH_ap				✓	
IH_ml				✓	
IH_v				✓	
rr_ap				✓	
det_ap		✗	✗		✓
AvgL_ap		✗	✗		✓
MaxL_ap		✗	✗		✓
Div_ap		✗	✗		✓
rr_ml				✓	
det_ml		✗	✗		✓
AvgL_ml		✗	✗		✓
MaxL_ml		✗	✗		✓
Div_ml		✗	✗		✓
rr_v				✓	
det_v		✗	✗		✓
AvgL_v		✗	✗		✓
MaxL_v		✗	✗		✓
Div_v		✗	✗		✓
sLE_ap				✓	
lLE_ap				✓	
sLE_ml				✓	
lLE_ml				✓	
sLE_v				✓	
lLE_v				✓	
sLE_tot				✓	
lLE_tot				✓	
SEN_ap				✓	
SEN_ml				✓	
SEN_v				✓	

Table 3: ✗ indicates presence of sample or frequency effects (first and second column) and ability of the interpolation process to solve the sample effect (third column). ✓ indicates in which condition the under-sampling is eligible.

3.5 DISCUSSION

The understanding and assessment of gait stability is a fundamental step to identify the subject's risk of falling [1]. Several variability and stability indexes have been proposed for the subject specific assessment of fall risk, demonstrating [2,3] capability to provide indication regarding the specific subject alterations increasing fall risk, potentially leading to a better insight in the functional analysis of gait pattern. Even though promising results were found, several variability and stability indexes require a high number of strides, a clinical issue, in order to guarantee an acceptable reliability [4] of the measure. For an effective exploitation of this approach in clinical practice, the continuous monitoring of subjects at risk is needed. In this respect smartphone is the ideal device for this goal. Although the IMUs mounted on smartphones have nothing to envy to other commercially available devices, they do not support high (i.e. above 100 Hz) sampling frequency. The influence of a reduced sampling frequency, usually at 50 Hz for Android systems [9], could not be *a priori* evaluable and negligible, also given the nonlinear nature of the variability and stability indexes. Consequently, the aim of the present study was to evaluate the influence of a reduced sampling frequency (from 128 Hz to 42.6 Hz) in the computation of stability and variability indexes, used for gait assessment.

From the signal theory it is known that an under-sampling process implies, in general, two effects on the under sampled signal:

- Reduced number of sample (*sample effect*)
- Different frequency content (*frequency effect*)

In this study both the above-mentioned effects were evaluated, together with a possible strategy based on the interpolation process to solve the sample effect.

The results showed that all the variability indexes were influenced neither by the sample effect, nor by the frequency one. This finding is not surprising since the variability indexes were performed on the stride time data. Stride time was estimated from the angular velocity around the medio-lateral axis of the ankle

[12], which even filtered at 20 Hz preserves its natural periodicity needed for the stride time calculations.

The stability indexes showed two different behaviours that converge into the same results: the decrease of sampling frequency from 128 to 42.6 Hz did not influence them. In details, the stability indexes that analysed the frequency content of the signal (i.e. HR and MSE) were influenced neither by the frequency, nor by the sample effect. This could be explained because the frequency content of the signal at the 95% was guaranteed [Chapter 2]. Moreover, when considering the MSE only coarse-grained coherent comparisons were performed. $\tau = 3$ and 6 for the original signal ($f_s = 128$ Hz) were compared to coarse-grained procedure with $\tau = 1$ and 2 for the under sampled ($f_{s\_UNDER} = f_s/3 = 42.6$ Hz) one. Indeed, operating a three times coarse-grain procedure from a signal sampled at 128 Hz would filter frequencies higher than 42.6 Hz, namely the frequency content of the under sampled signal (i.e. $\tau = 1$); while operating six coarse grain procedures on a signal sampled at 128 Hz or two coarse grain procedures from a sampling frequency of 42.6 Hz would filter frequencies higher than 21.3 Hz [18].

The stability indexes that analyse the time domain (see detail in Chapter 1) can be split into two groups: one composed by the indexes (LE and rr in all the directions) not influenced by the under-sampling (either sample or frequency effects) and one composed by the indexes (det, AvgL, Max, and Div in all directions) influenced by the under-sampling (i.e. sample effect) overcame by the interpolation process.

As better explained in Chapter 1 these indexes are based on the space state reconstruction through the delay embedding technique [19]. The time delay (i.e. lag) and embedding dimension (i.e. eD) were tuned accordingly for all the analysed signals (i.e. original, filtered, under sampled, and interpolated). This coherent setting of parameters (sampling frequency related) led to avoid influence of the reduced sampling frequency. This is not completely true for the features of the recurrence plot with the exception of the recurrence rate (rr).

The recurrence plot of the under sampled signal has dimension lower (i.e. three times less) than the acquired one; consequently it might influence the evaluated structures (e.g. diagonal line). Instead, the rr is not influenced by this

dimension reduction likely due to its intrinsic definition (i.e. as the ratio between the recurrence points and all the recurrence plot's points).

This study highlight that down-sampling (at 42.6 Hz) is feasible, if specific constraints are taken into account in the implementation of the analysed indexes. One possible limitation, given the many comparisons performed simultaneously, is type I error (multiple comparison problem). Although, several comparisons were performed to investigate different features of gait (variability and stability), when assessing similar aspects (e.g. variability) or when the same analysis approach (e.g. frequency domain analysis, or time domain analysis) was used, equal behaviours were obtained, thus reinforcing the results.

In conclusion this study highlights that the under-sampling process at 42.6 Hz is not compromising the evaluation of the fall risk monitoring from the laboratory to a portable device. However, these results cannot be generalized to other under-sampling frequency (lower than 42.6 Hz), assuming that frequency content below 20 Hz and a decrease of the number of samples will influence the indexes calculation.

3.6 REFERENCES:

[1] J.M. Hausdorff, D.A. Rios, H.K. Edelberg, Gait variability and fall risk in community-living older adults: A 1-year prospective study, Arch. Phys. Med. Rehabil. 82 (2001) 1050–1056. doi:10.1053/apmr.2001.24893.

[2] F. Riva, M.J.P. Toebes, M. Pijnappels, R. Stagni, J.H. van Dieën, Estimating fall risk with inertial sensors using gait stability measures that do not require step detection, Gait Posture. 38 (2013) 170–174. doi:10.1016/j.gaitpost.2013.05.002.

[3] F. Riva, P. Tamburini, A. Coni, R. Stagni, Motor stability evaluation in elderly subjects through instrumental stability measures and clinical rating scales, Gait Posture. 42, Supplement 3 (2015) S48–S49. doi:10.1016/j.gaitpost.2015.03.088.

[4] F. Riva, M.C. Bisi, R. Stagni, Gait variability and stability measures: Minimum number of strides and within-session reliability, Comput. Biol. Med. 50 (2014) 9–13. doi:10.1016/j.compbiomed.2014.04.001.

[5] R.J. Ellis, Y.S. Ng, S. Zhu, D.M. Tan, B. Anderson, G. Schlaug, Y. Wang, A Validated Smartphone-Based Assessment of Gait and Gait Variability in Parkinson's Disease, PLoS ONE. 10 (2015). doi:10.1371/journal.pone.0141694.

[6] M. Mancini, A. Salarian, P. Carlson-Kuhta, C. Zampieri, L. King, L. Chiari, F.B. Horak, ISway: a sensitive, valid and reliable measure of postural control, J. NeuroEngineering Rehabil. 9 (2012) 59. doi:10.1186/1743-0003-9-59.

[7] M. El-Gohary, S. Pearson, J. McNames, M. Mancini, F. Horak, S. Mellone, L. Chiari, Continuous Monitoring of Turning in Patients with Movement Disability, Sensors. 14 (2013) 356–369. doi:10.3390/s140100356.

[8] A. Kos, S. Tomažič, A. Umek, Evaluation of Smartphone Inertial Sensor Performance for Cross-Platform Mobile Applications, Sensors. 16 (2016). doi:10.3390/s16040477.

[9] T. Isho, H. Tashiro, S. Usuda, Accelerometry-Based Gait Characteristics Evaluated Using a Smartphone and Their Association with Fall Risk in People with Chronic Stroke, J. Stroke Cerebrovasc. Dis. 24 (2015) 1305–1311. doi:10.1016/j.jstrokecerebrovasdis.2015.02.004.

[10] B. Sun, Y. Wang, J. Banda, Gait Characteristic Analysis and Identification Based on the iPhone's Accelerometer and Gyrometer, Sensors. 14 (2014) 17037–17054. doi:10.3390/s140917037.

[11] N.A. Capela, E.D. Lemaire, N. Baddour, Novel algorithm for a smartphone-based 6-minute walk test application: algorithm, application development, and evaluation, J. NeuroEngineering Rehabil. 12 (2015). doi:10.1186/s12984-015-0013-9.

[12] K. Aminian, B. Najafi, C. Büla, P.-F. Leyvraz, P. Robert, Spatio-temporal parameters of gait measured by an ambulatory system using miniature gyroscopes, J. Biomech. 35 (2002) 689–699. doi:10.1016/S0021-9290(02)00008-8.

[13] J.M. Hausdorff, M.E. Nelson, D. Kaliton, J.E. Layne, M.J. Bernstein, A. Nuernberger, M.A.F. Singh, Etiology and modification of gait instability in older adults: a randomized controlled trial of exercise, J. Appl. Physiol. 90 (2001) 2117–2129.

[14] A.H. Khandoker, S.B. Taylor, C.K. Karmakar, R.K. Begg, M. Palaniswami, Investigating Scale Invariant Dynamics in Minimum Toe Clearance Variability of the Young and Elderly During Treadmill Walking, IEEE Trans. Neural Syst. Rehabil. Eng. 16 (2008) 380–389. doi:10.1109/TNSRE.2008.925071.

[15] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration patterns of the head and pelvis when walking on level and irregular surfaces, Gait Posture. 18 (2003) 35–46. doi:10.1016/S0966-6362(02)00159-5.

[16] M.T. Rosenstein, J.J. Collins, C.J. De Luca, A practical method for calculating largest Lyapunov exponents from small data sets, Phys. Nonlinear Phenom. 65 (1993) 117–134. doi:10.1016/0167-2789(93)90009-P.

[17] M.A. Riley, R. Balasubramaniam, M.T. Turvey, Recurrence quantification analysis of postural fluctuations, Gait Posture. 9 (1999) 65–78. doi:10.1016/S0966-6362(98)00044-7.

[18] M. Costa, C.-K. Peng, A. L. Goldberger, J.M. Hausdorff, Multiscale entropy analysis of human gait dynamics, Phys. Stat. Mech. Its Appl. 330 (2003) 53–60. doi:10.1016/j.physa.2003.08.022.
[19] L. Noakes, The takens embedding theorem, Int. J. Bifurc. Chaos. 01 (1991) 867–872. doi:10.1142/S0218127491000634.

Chapter 4

MOVING FROM LABORATORY TO REAL LIFE CONDITIONS: INFLUENCE ON THE ASSESSMENT OF VARIABILITY AND STABILITY OF GAIT[1]

"You've got the key of the street"
Charles Dickens, The Pickwick Papers

"Il camminare presuppone che
a ogni passo il mondo cambi
in qualche suo aspetto e pure
che qualcosa cambi in noi"
Italo Calvino, I mille giardini

[1]Published. *Moving from laboratory to real life conditions: Influence on the assessment of variability and stability of gait*. Tamburini P, Storm F, Buckley C, Bisi MC, Stagni R, Mazzà C. Gait & Posture 59 (2018) 248–252

4. MOVING FROM LABORATORY TO REAL LIFE CONDITIONS: INFLUENCE ON THE ASSESSMENT OF VARIABILITY AND STABILITY OF GAIT

4.1 ABSTRACT

The availability of wearable sensors allows shifting gait analysis from the traditional laboratory settings, to daily life conditions. However, limited knowledge is available about whether alterations associated to different testing environment (e.g. indoor or outdoor) and walking protocols (e.g. free or controlled), result from actual differences in the motor behaviour of the tested subjects or from the sensitivity to these changes of the indexes adopted for the assessment. In this context, it was hypothesized that testing environment and walking protocols would not modify motor control stability in the gait of young healthy adults, who have a mature and structured gait pattern, but rather the variability of their motor pattern.

To test this hypothesis, data from trunk and shank inertial sensors were collected from 19 young healthy participants during four walking tasks in different environments (indoor and outdoor) and in both controlled (i.e. following a predefined straight path) and free conditions. Results confirmed what hypothesized: variability indexes (Standard deviation, Coefficient of variation and Poincaré plots) were significantly influenced by both environment and walking condition. Stability indexes (Harmonic ratio, Short term Lyapunov exponents, Recurrence quantification analysis and Sample entropy), on the contrary, did not highlight any change in the motor control.

In conclusion, this study highlighted an influence of environment and testing condition on the assessment of specific characteristics of gait (i.e.

variability and stability). In particular, for young healthy adults, both environment and testing condition affect gait variability indexes, whereas neither affect gait stability indexes.

Key words: *daily life gait; variability indexes; stability indexes; indoor and outdoor walking; inertial sensors; accelerometers.*

4.2 INTRODUCTION

ABBREVIATIONS

SD	Standard Deviation
CV	Coefficient of Variation
PSD1	Short term variability of stride estimated *via* Poincaré plots
HR	Harmonic Ratio
HR_v	Harmonic Ratio computed on the vertical acceleration direction
HR_ml	Harmonic Ratio computed on the medio-lateral acceleration direction
HR_ap	Harmonic Ratio computed on the antero-posterior acceleration direction
sLE	Short term Lyapunov Exponent
sLE_v	Short term Lyapunov Exponent on the vertical acceleration direction
sLE_ml	Short term Lyapunov Exponent on the medio-lateral acceleration direction
sLE_ap	Short term Lyapunov Exponent on the antero-posterior acceleration direction
RQA	Recurrence Quantification Analysis
RR	Recurrence Rate
DET	Determinism
AvgL	Averaged diagonal line length
SEN	Sample entropy
SEN_v	Sample entropy on the vertical acceleration direction
SEN_ml	Sample entropy on the medio-lateral acceleration direction
SEN_ap	Sample entropy on the antero-posterior acceleration direction

Laboratory assessment has been the standard setting for quantitative gait analysis for several decades. However, in recent years, the availability of wearable inertial measurement units has allowed to quantitatively and easily assess gait also out of the lab [1,2].

The assessment of gait out of the laboratory, whereby it is not constrained to a predefined path, aims at reproducing a testing condition more similar to that of daily living. This type of assessment is particularly interesting for the investigation of gait performance and of the underlying motor control with a specific focus on the quantification of dynamic stability and fall risk. It can potentially overcome the limitations (e.g. limited acquired number of stride) of data acquired in laboratory conditions [2]. Moreover, the monitoring of gait, as obtained from various types of quantitative descriptive indexes, provides information that can significantly impact the design of more effective training and rehabilitative interventions [3].

Several studies [2,4,5] analysed the gait pattern of faller and non-faller elderly and pathological subjects in daily-living conditions using indexes assumed to quantify the motor performance and the underlying motor control. However, limited knowledge is available regarding if and how the testing environment (e.g. indoor or outdoor) and the imposition of a specific walking path (e.g. free or controlled) might affect gait pattern and performance, and whether the indexes, commonly adopted to quantify these aspects, are sensitive to these changes.

Therefore, it is crucial to understand whether the alterations, associated to different testing conditions, result from actual differences in the motor behaviour of the analysed subjects or rather from the sensitivity of the indexes adopted for the assessment.

It is almost impossible to infer this knowledge analysing elderly and/or pathologic subjects, however for young healthy subjects, it can be assumed that the motor control of a mature and structured gait pattern [6], will not be significantly affected by the testing conditions. Therefore, environmental and testing conditions are not expected to modify the motor control stability in the gait of a young healthy adult, who has the ability to face far more challenging conditions, but changes in the variability of the motor pattern could be expected as an adaptation to the environment in order to maintain stability.

The definition and applicability of the concepts of variability and stability is well defined in mechanics, while the two are often used addressing similar meanings in gait analysis referring to motor control. On one hand, in a complex dynamic system as human gait, variability could arise from the deterministic dynamics of the system (e.g. when a chaotic attractor is present as in human gait [7]). It follows that the measured variability is a reflection of the multiple degrees of freedom of the system and does not necessarily imply destabilization of the system itself [7]. On the other hand, stability could arise from both the intrinsic properties of the system (i.e. motor control) and the specific movement pattern (i.e. gait) [7,8].

It could be argued that while gait variability is an indirect assessment of the motor control through gait performance (e.g. stride time), stability is instead a direct evaluation of the performance of the underlying motor control [7–9].

Besides traditional approaches based on the quantification of mechanical features of gait [10], a number of indexes have been proposed to quantify aspects more related to motor control [11,12]. These indexes can be generally grouped as variability (i.e. standard deviation, coefficient of variation, Poincaré plots) and stability indexes (i.e. Lyapunov exponents, harmonic ratio, sample entropy and recurrence quantification analysis) [11], based on their mathematical implementation and which characteristics of the analysed signal they are expected to quantify.

According to the above mentioned concepts of variability and stability, variability indexes, usually applied on stride time data, are meant to assess changes in the peripheral realization of the gait pattern [7–9,13], whereas stability indexes, usually applied on trunk acceleration data, are meant to assess the stability of the trajectory of the centre of mass. Indeed, recent studies [9,14,15], analysing both healthy (from 4 years-old children to 25 years-old young adults) and pathological subjects (stroke), analysed the role of the variability in joint kinematics in determining a successful control of the stability of the centre of mass trajectory, approximated by the lower trunk [7,16,17]. Stride time and trunk acceleration data are two manifestations of the same control system in healthy and pathologic subjects [18,19].

With this differentiation in mind, and since healthy young subjects have a well achieved and stabilized gait pattern [6], our hypothesis is that, when testing young healthy subjects walking along both controlled and free paths, the indexes related to motor stability are not expected to be significantly affected. Conversely, modifications should be observed in variability indexes, due to the possibility to adjust the gait pattern to the environment in order to maintain stability.

In particular, an increase in variability indexes both from indoor to outdoor and from controlled to free conditions is expected, while no significant changes in gait stability indexes should be observed.

The present study aims at testing this hypothesis evaluating the influence of environment (indoor and outdoor) and testing conditions (controlled and free) on gait assessment when using variability and stability indexes in a young healthy population.

4.3 MATERIALS and METHODS

In a cross-over study, nineteen healthy young volunteers (5 females, 14 males, 28±3 years, 1.75±0.09 m, 72.0±9.2 kg) were recruited after having provided informed consent. Only subjects with no self-reported history of locomotor disturbances or injuries that could affect their normal walking behaviour, or cause fatigue during the experimental protocol were included in the study. The University of Sheffield's Research Ethics Committee granted ethical approval for the study.

Subjects wore two inertial measurement units (Opal, APDM, USA): one located on the lower trunk on the fifth lumbar vertebra, and one attached frontally on the right shank, 2 cm above the lateral malleolus, for stride detection [10]. Measures of accelerations of the trunk and angular velocity of the right shank were recorded at 128 Hz.

Subjects completed four walking tasks in two different environments (indoor and outdoor) and in both controlled (i.e. following a predefined straight path) and free conditions (see details in Table 1) [20], indicated as ICW (Indoor Controlled Walking), OCW (Outdoor Controlled Walking), IFW (Indoor Free Walking) and OFW (Outdoor Free Walking), respectively. All participants performed the walking task in the different testing conditions, in one day, following the same order: OCW, OFW, IFW, ICW.

CONDITION	ACRONYM	DESCRIPTION	DURATION /REPETITIONS
Indoor controlled walking	ICW	Walking at preferred speed along an indoor straight path 20.0 m long walkway.	Eight repetitions.
Outdoor controlled walking	OCW	Walking at preferred speed along an outdoor straight path 50.0 m long walkway.	Six repetitions.
Indoor free walking	IFW	Walking along corridors within a university building, avoiding stairs.	Two minutes.
Outdoor free walking	OFW	Walking along footpaths open to the public in the city centre without any restrictions in route or walking speed, avoiding stairs.	Fifteen minutes.

Table 1: Summary of the walking conditions performed during the experimental protocol, with acronym, description, and duration or repetition [20].

- ICW was performed in a quiet corridor of the university building, and participants were asked to walk on a straight line for 20 m. The distance was measured and marked on the floor using adhesive tape.
- For IFW condition, participants were instructed to walk inside the university corridors starting from the main entrance, with no restriction of route, opening and closing doors as necessary. The data was always collected during normal working hours, in mostly busy corridors.
- OCW was performed in a quiet open space within the university premises, on a flat tarmac surface.
- For OFW, participants were instructed to walk freely in the city centre, with no restrictions regarding route or walking speed, but avoiding stairs.

During IFW and OFW the participants did not have verbal interaction with other people, but they may have had to adjust their gait due to the presence of others in the surroundings. Interactions with other people were possible, particularly during IFW. Finally, during IFW and OFW turns could also be recorded in addition to straight walking. However, turns and resting periods were segmented and excluded from the analysis. Turn events with durations between 1-3 stride time and angles around the vertical axis over 40° were identified and removed using the method specified by El-Gohary et al. [21]. Resting periods were defined as those when the time between subsequent heel strikes [10] was higher than 1.5 s.

For each participant and each condition 80 strides were analysed, since this was the maximum number of strides available in all conditions.

Gait variability was assessed on stride times using the variability indexes:

- Standard Deviation (SD)
- Coefficient of Variation (CV) [22]
- Short term variability of stride estimated *via* Poincaré plots (PSD1) [23].

Gait stability was assessed applying to the vertical (v), medio-lateral (ml), and antero-posterior (ap) trunk acceleration components the stability indexes:

- Harmonic Ratio (HR_v, HR_ap, HR_ml) [24] (see Chapter 1 for more details);
- Short term Lyapunov exponents (sLE_v, sLE_ap, sLE_ml) [25,26] (see Chapter 1 for more details);
- Recurrence quantification analysis (RQA) implying the calculation of recurrence rate (RR), determinism (DET) and averaged diagonal line length (AvgL) [27] (see Chapter 1 for more details);
- Sample entropy (SEN_v, SEN_ml and SEN_ap) [28] (see Chapter 1 for more details).

These indexes were selected, among those previously used to detect changes in the gait pattern [4,12,29,30], based on the available number of consecutive strides per trial, which would ensure a reliability of at least 20% [11,31]. Raw unfiltered data were analysed to assure that information was not lost or altered.

Matlab R2015b (MathWorks BV, USA) was used for data and statistical analysis.

A Shapiro-Wilk test was performed on all the above-mentioned indexes, showing that they were not normally distributed. Median, 25^{th} and 75^{th} percentile values were hence calculated. Kruskal-Wallis test with minimum level of significance of 5% was performed to compare the indexes values obtained in the different walking conditions. Dunn-Sidak correction was considered for post-hoc analysis.

4.4 RESULTS

Figure 1 shows a representative time series of trunk acceleration in the antero-posterior direction and the angular velocity of the shank around the medio-lateral axis for each condition.

All variability indexes varied significantly between the analysed walking conditions, conversely from the stability indexes (with the only exception of HR in both v and ap) as shown in Figure 2. In particular, the Kruskal-Wallis test showed statistically significant differences for PSD1 between OCW and OFW and between ICW and OFW, with values 35% higher in OFW than in OCW and ICW.

SD and CV in ICW were significantly different from both OCW and OFW conditions, being approximately 20% lower.

Despite the fact that HR_v and HR_ap significantly diminished when moving from ICW to OFW, the observed numerical differences were lower than the known reliability thresholds of this indexes [11]. Similarly, significant but not reliable variations were observed for HR_ap between OFW and OCW and between OFW and IFW.

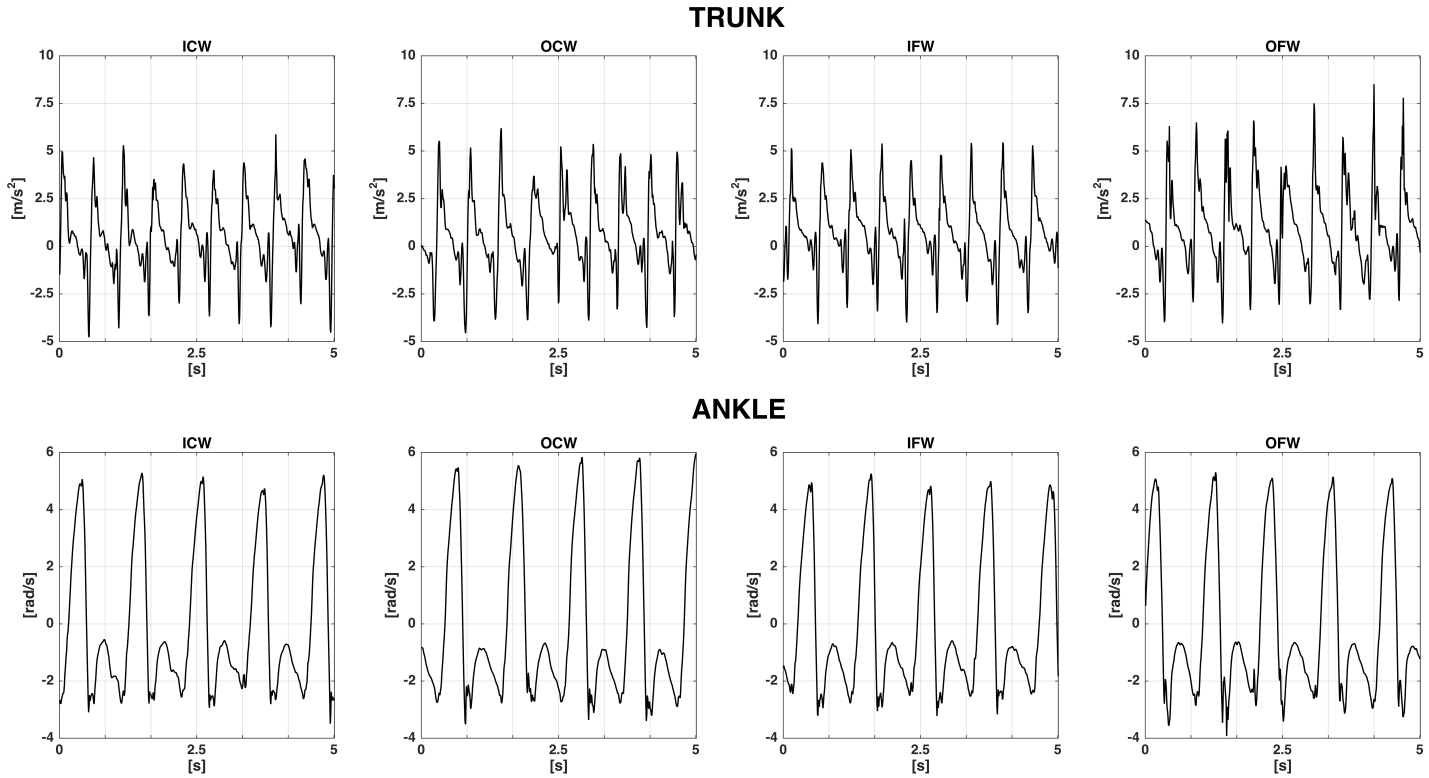

Figure 1: First line: representative trunk acceleration signal in antero-posterior direction in the four (ICW, OCW, IFW and OFW) walking conditions. Second line: representative angular velocity of the shank around the medio-lateral axis in the four (ICW, OCW, IFW and OFW) walking conditions.

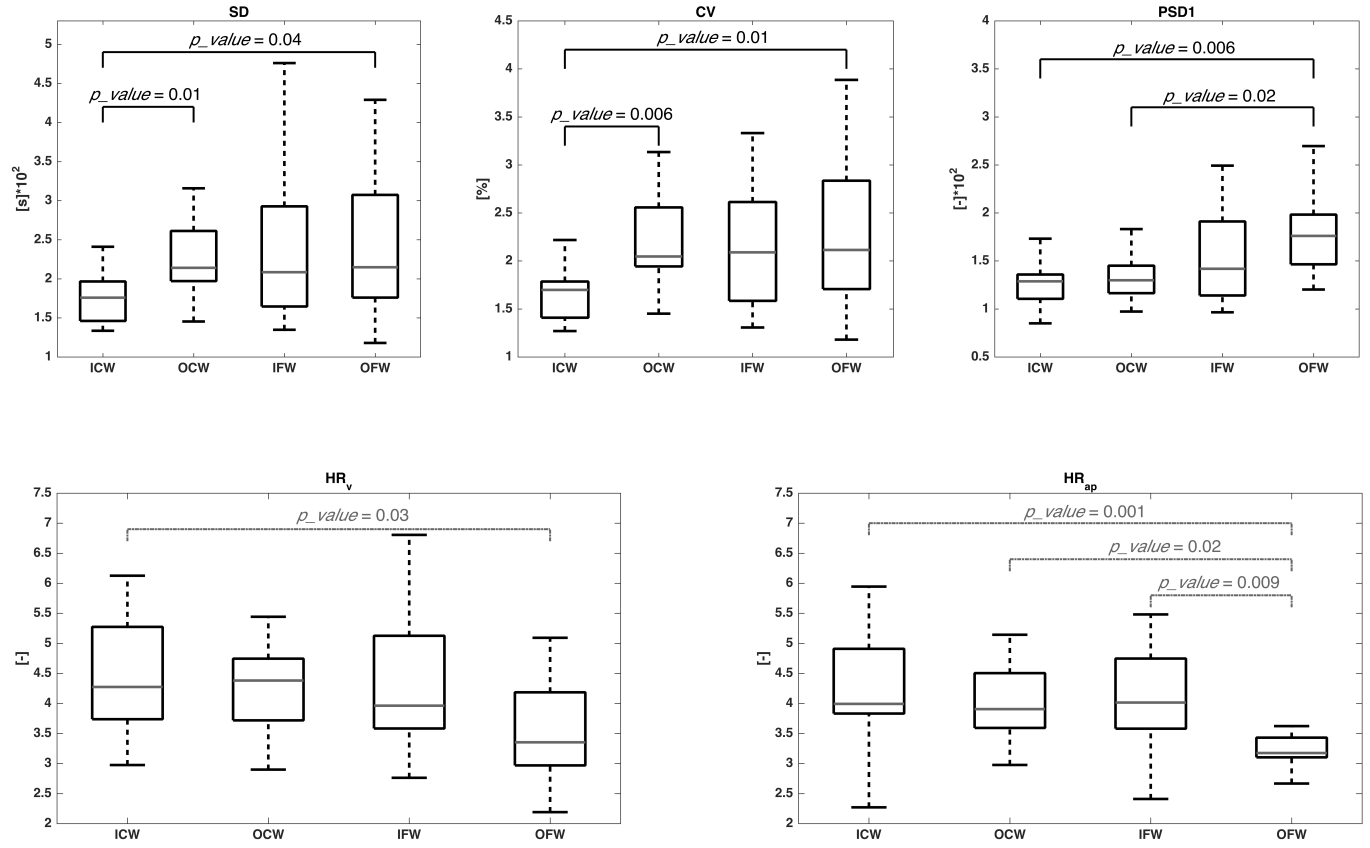

Figure 2: Median, 25th and 75th percentiles and the *p_value* of variability and stability indexes results showing significant differences (*p_value*<5%) for the four walking conditions (ICW, OCW, IFW and OFW). Grey dotted lines indicate significant differences below the index reliability that can be associated to the analysed number of strides [11].

4.5 DISCUSSION

The walking pattern of young healthy adults was analysed in different environments (indoor and outdoor) and testing conditions (controlled and free) to assess if and how variability and stability, quantified using commonly used variability and stability indexes [11], would be affected. The hypothesis in the specific population was that stability would not change significantly, while variability would increase moving from indoor to outdoor and from controlled to free condition.

Overall, the results confirmed the study hypothesis: on one hand variability indexes, associated to the specific gait pattern, can be altered by testing conditions; on the other hand, stability indexes, related to the underlying motor control, are influenced neither by the environmental nor by the type of walking.

The differences observed in SD e CV values between Indoor Controlled Walking (ICW) and Outdoor Free Walking (OFW) indicate that stride time variability changes significantly when moving from the laboratory to outdoor walking conditions. This was further confirmed by the PSD1 values: both observed differences (ICW *vs* OFW and OCW *vs* OFW) and the trend (increased values from indoor controlled condition to the outdoor free one) highlighted how short-term variability of stride times [23] should be interpreted with caution when analysing data from different environments and testing conditions.

The variability indexes were influenced also by the environment in the controlled walking (ICW *vs* OCW): it has to be acknowledged that besides the change in the environment, differences in the length of the path in the two walking conditions can also affect gait variability, as suggested for older subjects [32].

No significant difference was found in stability indexes, in accordance with the study hypothesis. SEN showed similar values for all testing conditions, moreover the observed trends, in all directions, are in accordance to those reported in the literature [4,33]: higher SEN values for increasing τ. This further supports the study hypothesis, highlighting how the stability of trunk acceleration during

gait is not influenced by testing conditions and environment in young healthy adults.

The increase in gait variability, associated to different testing conditions of gait in healthy young adults, suggests that this behaviour should not always be considered as a warning symptom, as usually interpreted for elderly subjects [34]. Changes in variability are not necessarily related to a reduction of gait stability, hence not necessarily to be interpreted as an increase in fall risk.

Given the many comparisons performed simultaneously, type I errors (multiple comparison problem) are deemed possible. However, in the present study, several comparisons were performed to investigate different aspects of gait control and, when assessing similar aspects (e.g. variability), the same trends were obtained from different parameters, thus reinforcing the results. In addition, a bias could have been introduced by the choice of performing the four walking tasks in the same order. However, both the homogeneity of the results (similar analysed aspects showed same behaviour) and, when present, highly significant differences ($p\_value << 5\%$) suggest the potential bias to be marginal, if not negligible.

In conclusion, this study highlighted the influence of environment and testing condition in the assessment of specific characteristics of gait (i.e. variability and stability). In particular, when assessing the gait of young healthy adults, both environment and testing condition affect variability indexes, whereas neither of the two affects stability indexes.

In general, these results cannot be generalized to other populations, assuming that testing in or out of the lab will not affect gait stability assessment, for instance, in elderly and/or pathologic subjects. Nevertheless, the eventual assessment of significant differences in stability indexes, quantified for indoor and outdoor walking conditions in elderly and/or pathologic populations, would suggest an increased frailty of these subjects in terms of motor stability and fall risk, when compared to the reference performance of young healthy adults.

4.6 ACKNOWLEDGEMENTS

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4.7 SUPPLEMENTARY MATERIAL

Index		Walking conditions				Statistical significance (p_value<5%)
		ICW	OCW	IFW	OFW	
SD [s*10^{-2}]	**Median**	1,76	2,16	2,08	2,15	ICW vs OCW and ICW vs OFW
	(25th-75th)	(1,46-1,97)	(1,97-2,61)	(1,65-2,93)	(1,76-3,08)	
CV%	**Median**	1,70	2,07	2,09	2,11	ICW vs OCW and ICW vs OFW.
	(25th-75th)	(1,41-1,79)	(1,94-2,56)	(1,58-2,61)	(1,71-2,84)	
PSD1*10^{-2}	**Median**	1,29	1,30	1,42	1,76	ICW vs OFW and OCW vs OFW.
	(25th-75th)	(1,11-1,36)	(1,17-1,45)	(1,14-1,91)	(1,46-1,98)	
HR_v	**Median**	4,24	4,38	3,96	3,50	ICW vs OFW*
	(25th-75th)	(3,74-5,28)	(3,72-4,74)	(3,59-5,13)	(2,97-4,19)	
HR_ml	**Median**	2,17	2,24	2,22	2,00	
	(25th-75th)	(1,85-2,75)	(1,84-2,50)	(1,86-2,56)	(1,72-2,19)	
HR_ap	**Median**	3,99	3,91	4,01	3,26	OFW vs ICW*, IFW vs OFW* and OCW vs OFW*
	(25th-75th)	(3,83-4,91)	(3,60-4,51)	(3,58-4,75)	(3,10-3,43)	
sLE_v	**Median**	1,29	1,43	1,34	1,33	
	(25th-75th)	(1,13-1,52)	(1,28-1,57)	(1,18-1,52)	(1,15-1,50)	
sLEml	**Median**	0,88	1,01	0,84	0,78	
	(25th-75th)	(0,68-1,03)	(0,86-1,15)	(0,72-1,04)	(0,69-0,90)	
sLE_ap	**Median**	0,98	1,04	1,01	0,89	
	(25th-75th)	(0,82-1,20)	(0,82-1,28)	(0,87-1,25)	(0,73-1,12)	
RR_v	**Median**	13,99	14,21	14,38	14,78	
	(25th-75th)	(12,77-15,02)	(12,74-15,61)	(12,83-14,89)	(13,59-17,25)	
DET_v	**Median**	82,39	81,10	81,41	84,30	
	(25th-75th)	(76,61-85,45)	(75,81-83,83)	(77,76-86,24)	(75,61-86,67)	

Index		Walking conditions				Statistical significance (p_value<5%)
		ICW	OCW	IFW	OFW	
AvgL_v	**Median** (25th-75th)	11,69 (10,29-13,24)	11,81 (11,02-13,28)	12,42 (10,73-13,28)	12,31 (10,14-13,17)	
RR_ml	**Median** (25th-75th)	9,07 (7,84-10,70)	8,59 (7,93-9,75)	8,66 (8,03-9,51)	7,96 (7,56-8,93)	
DET_ml	**Median** (25th-75th)	47,83 (40,73-57,71)	47,67 (37,87-54,78)	48,69 (41,18-57,04)	42,35 (37,41-48,94)	
AvgL_ml	**Median** (25th-75th)	6,46 (6,01-6,92)	6,21 (6,10-6,95)	6,44 (5,91-6,95)	5,99 (5,72-6,39)	
RR_ap	**Median** (25th-75th)	15,37 (15,00-15,92)	15,67 (14,38-16,75)	15,71 (14,67-16,44)	14,74 (13,89-16,24)	
DET_ap	**Median** (25th-75th)	74,99 (64,55-83,58)	78,96 (66,64-83,49)	73,43 (69,21-82,21)	71,53 (59,31-80,92)	
AvgL_ap	**Median** (25th-75th)	9,58 (7,65-10,38)	9,14 (7,45-9,59)	9,58 (7,87-10,07)	8,10 (7,29-8,98)	
SEN_v τ=1	**Median** (25th-75th)	0,33 (0,31-0,37)	0,32 (0,31-0,36)	0,35 (0,32-0,38)	0,36 (0,31-0,40)	
SEN_v τ=2	**Median** (25th-75th)	0,46 (0,42-0,51)	0,43 (0,40-0,52)	0,47 (0,44-0,49)	0,49 (0,43-0,54)	
SEN_v τ=3	**Median** (25th-75th)	0,57 (0,55-0,61)	0,55 (0,52-0,65)	0,61 (0,54-0,64)	0,59 (0,55-0,67)	
SEN_v τ=4	**Median** (25th-75th)	0,66 (0,63-0,75)	0,67 (0,64-0,78)	0,71 (0,64-0,77)	0,69 (0,65-0,83)	
SEN_v τ=5	**Median** (25th-75th)	0,72 (0,70-0,86)	0,79 (0,74-0,88)	0,78 (0,69-0,87)	0,84 (0,72-0,98)	
SEN_v τ=6	**Median** (25th-75th)	0,79 (0,72-0,92)	0,86 (0,75-0,98)	0,81 (0,76-0,95)	0,86 (0,74-1,03)	
SEN_ml τ=1	**Median** (25th-75th)	0,62 (0,50-0,69)	0,54 (0,47-0,62)	0,59 (0,52-0,65)	0,54 (0,49-0,62)	
SEN_ml	**Median**	0,85	0,80	0,85	0,81	

Index		Walking conditions				Statistical significance (p_value<5%)
		ICW	OCW	IFW	OFW	
τ=2	(25th-75th)	(0,72-0,99)	(0,64-0,94)	(0,78-1,00)	(0,68-0,91)	
SEN_ml τ=3	Median	0,99	0,97	1,05	1,01	
	(25th-75th)	(0,89-1,24)	(0,81-1,14)	(0,89-1,17)	(0,85-1,17)	
SEN_ml τ=4	Median	1,15	1,06	1,26	1,19	
	(25th-75th)	(1,00-1,36)	(0,94-1,24)	(1,01-1,35)	(1,03-1,35)	
SEN_ml τ=5	Median	1,29	1,21	1,42	1,33	
	(25th-75th)	(1,04-1,44)	(1,09-1,33)	(1,11-1,48)	(1,16-1,53)	
SEN_ml τ=6	Median	1,37	1,30	1,44	1,40	
	(25th-75th)	(1,16-1,45)	(1,19-1,45)	(1,24-1,53)	(1,26-1,66)	
SEN_ap τ=1	Median	0,32	0,28	0,35	0,31	
	(25th-75th)	(0,30-0,38)	(0,26-0,35)	(0,29-0,40)	(0,26-0,37)	
SEN_ap τ=2	Median	0,44	0,42	0,43	0,44	
	(25th-75th)	(0,37-0,52)	(0,38-0,49)	(0,39-0,52)	(0,39-0,53)	
SEN_ap τ=3	Median	0,51	0,54	0,50	0,55	
	(25th-75th)	(0,45-0,63)	(0,45-0,58)	(0,44-0,64)	(0,49-0,66)	
SEN_ap τ=4	Median	0,60	0,60	0,60	0,64	
	(25th-75th)	(0,51-0,69)	(0,53-0,71)	(0,51-0,71)	(0,59-0,77)	
SEN_ap τ=5	Median	0,63	0,64	0,66	0,76	
	(25th-75th)	(0,57-0,73)	(0,59-0,81)	(0,57-0,73)	(0,69-0,86)	
SEN_ap τ=6	Median	0,65	0,69	0,67	0,75	
	(25th-75th)	(0,62-0,79)	(0,64-0,80)	(0,63-0,77)	(0,68-0,85)	

Table 3: Median, 25th and 75th percentiles of variability and stability indexes results obtained for the four walking conditions (ICW, OCW, IFW and OFW). Significant differences (p_value<5%): asterisks (*) indicate differences below the indexes reliability that can be associated to the analyzed number of strides [11].

4.8 REFERENCES

[1] B. J, U.W. Ebner-Priemer, J. Fahrenberg, Ambulatory activity monitoring: Progress in measurement of activity, posture, and specific motion patterns in daily life, Eur. Psychol. 14 (2009) 142–152. doi:10.1027/1016-9040.14.2.142.

[2] A. Weiss, M. Brozgol, M. Dorfman, T. Herman, S. Shema, N. Giladi, J.M. Hausdorff, Does the evaluation of gait quality during daily life provide insight into fall risk? A novel approach using 3-day accelerometer recordings, Neurorehabil. Neural Repair. 27 (2013) 742–752. doi:10.1177/1545968313491004.

[3] B.H. Dobkin, A. Dorsch, The Promise of mHealth, Neurorehabil. Neural Repair. 25 (2011) 788–798. doi:10.1177/1545968311425908.

[4] E.A.F. Ihlen, A. Weiss, A. Bourke, J.L. Helbostad, J.M. Hausdorff, The complexity of daily life walking in older adult community-dwelling fallers and non-fallers, J. Biomech. 49 (2016) 1420–1428. doi:10.1016/j.jbiomech.2016.02.055.

[5] S. Del Din, A. Godfrey, C. Mazzà, S. Lord, L. Rochester, Free-living monitoring of Parkinson's disease: Lessons from the field, Mov. Disord. 31 (2016) 1293–1313. doi:10.1002/mds.26718.

[6] Understanding motor development : infants, children, adolescents, adults / David L. Gallahue, John C. Ozmun. - Version details, Trove. (n.d.). http://trove.nla.gov.au/version/36850867 (accessed November 30, 2016).

[7] S.M. Bruijn, O.G. Meijer, P.J. Beek, J.H. van Dieën, Assessing the stability of human locomotion: a review of current measures, J. R. Soc. Interface. 10 (2013). doi:10.1098/rsif.2012.0999.

[8] D. Hamacher, N.B. Singh, J.H. Van Dieën, M.O. Heller, W.R. Taylor, Kinematic measures for assessing gait stability in elderly individuals: a systematic review, J. R. Soc. Interface. 8 (2011) 1682–1698. doi:10.1098/rsif.2011.0416.

[9] E. Papi, P.J. Rowe, V.M. Pomeroy, Analysis of gait within the uncontrolled manifold hypothesis: Stabilisation of the centre of mass during gait, J. Biomech. 48 (2015) 324–331. doi:10.1016/j.jbiomech.2014.11.024.

[10] K. Aminian, B. Najafi, C. Büla, P.-F. Leyvraz, P. Robert, Spatio-temporal parameters of gait measured by an ambulatory system using miniature gyroscopes, J. Biomech. 35 (2002) 689–699. doi:10.1016/S0021-9290(02)00008-8.

[11] F. Riva, M.C. Bisi, R. Stagni, Gait variability and stability measures: Minimum number of strides and within-session reliability, Comput. Biol. Med. 50 (2014) 9–13. doi:10.1016/j.compbiomed.2014.04.001.

[12] D. Hamacher, D. Hamacher, N.B. Singh, W.R. Taylor, L. Schega, Towards the assessment of local dynamic stability of level-grounded walking in an older population, Med. Eng. Phys. 37 (2015) 1152–1155. doi:10.1016/j.medengphy.2015.09.007.

[13] J.B. Dingwell, J. John, J.P. Cusumano, Do humans optimally exploit redundancy to control step variability in walking?, PLoS Comput. Biol. 6 (2010) e1000856. doi:10.1371/journal.pcbi.1000856.

[14] M.C. Bisi, R. Stagni, Is CoM kinematics a descriptive parameter of gait motor development? Verification on children and adults, Gait Posture. 42 (2015) S100. doi:10.1016/j.gaitpost.2015.06.182.

[15] P. Tamburini, D. Mazzoli, R. Stagni, Towards an objective assessment of motor function in sub-acute stroke patients: Relationship between clinical rating scales and instrumental gait stability indexes, Gait Posture. 59 (2018) 58–64. doi:10.1016/j.gaitpost.2017.09.033.

[16] W. Zijlstra, A.L. Hof, Displacement of the pelvis during human walking: experimental data and model predictions, Gait Posture. 6 (1997) 249–262. doi:10.1016/S0966-6362(97)00021-0.

[17] K. Wilmut, W. Du, A.L. Barnett, Gait patterns in children with Developmental Coordination Disorder, Exp. Brain Res. 234 (2016) 1747–1755. doi:10.1007/s00221-016-4592-x.

[18] W. Zijlstra, A.L. Hof, Assessment of spatio-temporal gait parameters from trunk accelerations during human walking, Gait Posture. 18 (2003) 1–10. doi:10.1016/S0966-6362(02)00190-X.
[19] J. McCamley, M. Donati, E. Grimpampi, C. Mazzà, An enhanced estimate of initial contact and final contact instants of time using lower trunk inertial sensor data, Gait Posture. 36 (2012) 316–318. doi:10.1016/j.gaitpost.2012.02.019.
[20] F.A. Storm, C.J. Buckley, C. Mazzà, Gait event detection in laboratory and real life settings: Accuracy of ankle and waist sensor based methods, Gait Posture. 50 (2016) 42–46. doi:10.1016/j.gaitpost.2016.08.012.
[21] M. El-Gohary, S. Pearson, J. McNames, M. Mancini, F. Horak, S. Mellone, L. Chiari, Continuous Monitoring of Turning in Patients with Movement Disability, Sensors. 14 (2013) 356–369. doi:10.3390/s140100356.
[22] J.M. Hausdorff, M.E. Nelson, D. Kaliton, J.E. Layne, M.J. Bernstein, A. Nuernberger, M.A.F. Singh, Etiology and modification of gait instability in older adults: a randomized controlled trial of exercise, J. Appl. Physiol. 90 (2001) 2117–2129.
[23] A.H. Khandoker, S.B. Taylor, C.K. Karmakar, R.K. Begg, M. Palaniswami, Investigating Scale Invariant Dynamics in Minimum Toe Clearance Variability of the Young and Elderly During Treadmill Walking, IEEE Trans. Neural Syst. Rehabil. Eng. 16 (2008) 380–389. doi:10.1109/TNSRE.2008.925071.
[24] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration patterns of the head and pelvis when walking on level and irregular surfaces, Gait Posture. 18 (2003) 35–46. doi:10.1016/S0966-6362(02)00159-5.
[25] J.B. Dingwell, H.G. Kang, Differences Between Local and Orbital Dynamic Stability During Human Walking, J. Biomech. Eng. 129 (2006) 586–593. doi:10.1115/1.2746383.
[26] M.T. Rosenstein, J.J. Collins, C.J. De Luca, A practical method for calculating largest Lyapunov exponents from small data sets, Phys. Nonlinear Phenom. 65 (1993) 117–134. doi:10.1016/0167-2789(93)90009-P.
[27] M.A. Riley, R. Balasubramaniam, M.T. Turvey, Recurrence quantification analysis of postural fluctuations, Gait Posture. 9 (1999) 65–78. doi:10.1016/S0966-6362(98)00044-7.
[28] M. Costa, C.-K. Peng, A. L. Goldberger, J.M. Hausdorff, Multiscale entropy analysis of human gait dynamics, Phys. Stat. Mech. Its Appl. 330 (2003) 53–60. doi:10.1016/j.physa.2003.08.022.
[29] M.C. Bisi, R. Stagni, Development of gait motor control: what happens after a sudden increase in height during adolescence?, Biomed. Eng. OnLine. 15 (2016). doi:10.1186/s12938-016-0159-0.
[30] D. Hamacher, D. Hamacher, A. Törpel, M. Krowicki, F. Herold, L. Schega, The reliability of local dynamic stability in walking while texting and performing an arithmetical problem, Gait Posture. 44 (2016) 200–203. doi:10.1016/j.gaitpost.2015.12.021.
[31] B. Galna, S. Lord, L. Rochester, Is gait variability reliable in older adults and Parkinson's disease? Towards an optimal testing protocol, Gait Posture. 37 (2013) 580–585. doi:10.1016/j.gaitpost.2012.09.025.
[32] B. Najafi, J.L. Helbostad, R. Moe-Nilssen, W. Zijlstra, K. Aminian, Does walking strategy in older people change as a function of walking distance?, Gait Posture. 29 (2009) 261–266. doi:10.1016/j.gaitpost.2008.09.002.
[33] M.C. Bisi, R. Stagni, Complexity of human gait pattern at different ages assessed using multiscale entropy: From development to decline, Gait Posture. 47 (2016) 37–42. doi:10.1016/j.gaitpost.2016.04.001.
[34] J. Verghese, R. Holtzer, R.B. Lipton, C. Wang, Quantitative Gait Markers and Incident Fall Risk in Older Adults, J. Gerontol. A. Biol. Sci. Med. Sci. 64A (2009) 896–901. doi:10.1093/gerona/glp033.

Chapter 5

TOWARDS AN OBJECTIVE ASSESSMENT OF MOTOR FUNCTION IN SUB-ACUTE STROKE PATIENTS: RELATIONSHIP BETWEEN CLINICAL RATING SCALES AND INSTRUMENTAL GAIT STABILITY INDEXES[1]

"I just wondered how things were put together."
Claude Shannon

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5. TOWARDS AN OBJECTIVE ASSESSMENT OF MOTOR FUNCTION IN SUB-ACUTE STROKE PATIENTS: RELATIONSHIP BETWEEN CLINICAL RATING SCALES AND INSTRUMENTAL GAIT STABILITY INDEXES

5.1 ABSTRATC

The assessment of walking function alterations is a key issue to design effective rehabilitative interventions in sub-acute stroke patients. Nevertheless, the objective quantification of these alterations remains a challenge.

Clinical rating scales are commonly used in clinical practice, but have been proven prone to errors associated to the evaluator subjective perception. On the other hand, instrumental measurement of trunk acceleration can be exploited for an objective quantitative characterization of gait function, but it is not applied in routine clinical practice, because the resulting quantitative indexes have not been related to the clinically information, conventionally provided by the rating scales. To overcome this limitation, the relationship between the indexes, in specific clinical conditions, and rating scale must be better investigated, to support their exploitability in the clinical practice as a fast and reliable screening tool.

Thirty-one sub-acute stroke patients (17 with and 14 without cane) participated in the study. All were assessed with 6 rating scales (MI, TCT, MRI, FAC, WHS, CIRS) and 2 functional tests (2MWT and TUG). Sample Entropy (SEN) and Recurrence Quantification Analysis (RQA) in AP, ML and V directions were calculated over 2MWT and walking section of TUG. The

influence of assessment task and cane was analysed, as well as correlation of SEN and RQA indexes with clinical rating scales.

SEN and RQA on the medio-lateral plane resulted influenced by the use of the cane, while the correlations between indexes and clinical scales showed that SEN and RQA for antero-posterior direction correlate positively with WHS.

Key words: *Stability indexes; stroke; walking deficits; clinical scales; wearable sensors.*

5.2 INTRODUCTION

ABBREVIATIONS

NoCane	Sub-acute stroke patents with the ability to walk without cane
Cane	Sub-acute stroke patents, who needed additional support for walking
2MWT	2-Minute Walk Test
d_2MWT	Travelled distance during 2MWT
TUG	Timed-Up and Go Test
t_TUG	Execution time of the TUG
MI	Motricity Index
TCT	Trunk Control Test
RMI	Rivermead Mobility Index
FAC	Functional Ambulation Category
WHS	Walking Handicap Scale
CIRS	Cumulative Illness Rating Scale
SI	Severity Index
CI	Co-morbidity Index
RQA	Recurrence Quantification Analysis
RR	Recurrence Rate
DET	Determinism
AvgL	Averaged diagonal line length
SEN	Sample entropy
SEN_v	Sample entropy on the vertical acceleration direction
SEN_ml	Sample entropy on the medio-lateral acceleration direction
SEN_ap	Sample entropy on the antero-posterior acceleration direction

Sub-acute stroke patients are often affected by residual alterations of gait associated to an increased risk of fall [1,2]. These patients are identified, according to Sullivan [3], as those in between the acute and the chronic phase, in the continuous timeline starting on the stroke on-set until years post-stroke. Different symptoms (e.g. dystonia, spasticity, muscle weakness) may be observed during the evolution of the disease. Some of them (e.g. spasticity occurring in about 30% of patients [4]) have a highly variable onset and can occur in short-, medium- or long-term post-stroke period [5], interfering with the recovery of the ability to walk, to social participation and to autonomous living. The primary aim of the rehabilitation process is to restore and maintain the ability to perform actives of daily living, usually starting within the first days after the event and often continuing during the chronic stroke phase [6].

A recent review [7] has shown that, in the chronic stage, walk training resulted in increased walking speed and distance compared with no/placebo

treatment. Hence, restoring gait ability is not only a primary objective during the sub-acute phase, but a feature to be extended to all post stroke recovery stages. Therefore, the assessment of walking functional alterations is crucial to design an effective rehabilitative project. Unfortunately, the objective quantification of these alterations remains a challenge, not allowing to eventually discriminate patients, who retain some functional reserve and consequently could benefit from additional specific rehabilitation.

In clinical practice, the assessment of motor function is usually performed using rating scales and/or motor functional tests. In the perspective of a multi-dimensional rehabilitation process, these can assess patients through the International Classification of Functioning (ICF), which focuses on function, disability and contextual factors. Nevertheless, different clinical scales address different clinical aspects, can be time consuming and prone to inaccuracies and bias resulting from the subjective perception of the evaluator [8].

On the other hand, instrumental assessment of walking can provide an objective quantitative evaluation. In particular, indexes proposed for the quantification of gait stability, calculated on trunk acceleration, raised great interest in recent years. They have been proposed to provide a synthetic and easy to use method for the objective quantitative characterization of gait function, and have shown promising results in the assessment of walking deficits and fall risk in healthy elderly subjects [2,9–11].

Differently from clinical rating scales, these indexes are fast and easy to use, requiring only a few minutes for the acquisition of trunk accelerations during gait, and are not affected by intra-rate variability. Thus, they could serve as an effective screening tool for the identification of those subjects potentially retaining some functional reserve, who could benefit of additional specific clinical assessment and rehabilitation.

Nevertheless, the possible exploitation of these indexes for clinical use requires, first of all, to establish their relationship with clinical scales, the current standard for clinical assessment.

On the other hand, from a methodological point of view, it is also essential to analyse relevant aspects associated to the specific experimental assessment

conditions, since non-linear time series analysis often showed contradictory results and non-monotonic relationships due to their intrinsic non-linear nature, even when applied in the same context [12,13]. Therefore, it is important to understand the specific conditions, in which the indexes are applied.

In particular, for the specific acquisition of trunk acceleration data during gait, different functional tests, already applied in clinical practice, could be instrumented. Different tests used to assess endurance (e.g. 2-Minute Walk Test (2MWT) [14,15]) or mobility (e.g. Timed-Up and Go Test (TUG) [16,17], Balance Evaluation Systems Test [18]) and others include a walking task. Among these, 2MWT is certainly the one offering the steady walking condition usually referred to for the calculation of gait stability indexes [19], while the walking section of TUG [16,17] is usually shorter and included between two transient conditions (standing from a chair and a U-turn), thus potentially different in the perspective of motor control assessment, for stroke patients in particular. Nevertheless, TUG has already been instrumented for clinical practice [17] and proposed for this type of assessment.

In addition to this, stability indexes have already been proposed and analysed for normal gait [11,19], while a large number of stroke patients cannot walk without the support of a cane, which modifies ground reaction forces and consequently can modify trunk accelerations. From the point of view of non-linear analysis, both these aspects -tasks and populations characteristics- should be taken into account to implement a reliable analysis.

Therefore, the aim of the present study was: a) from a methodological point of view, to evaluate how the stability indexes are affected by the task used for the acquisition of trunk acceleration during gait (i.e. 2MWT *vs* TUG) and by the use of a support (i.e. *NoCane vs Cane*) in the reference target population of sub-acute stroke patients; b) in the perspective of possible clinical exploitation, to assess the relationship between instrumental gait stability indexes calculated on 2MWT and TUG and some of the most used clinical scales for the assessment of sub-acute stroke subjects (*NoCane* and *Cane*).

5.3 MATERIALS and METHODS

5.3.1 Study subjects

Thirty-one sub-acute stroke patients participated in the study, divided in two groups: *NoCane*, who were able to walk without a cane (53±10years, 70±11kg, 9males and 8females) and *Cane,* who required the support of a cane for walking (64±11years, 70±15kg, 9males and 5females).
Sub-acute stroke patients were selected based on clinical indication for the analysis, from 7 days following the stroke [3].

The inclusion criteria were: absence of cardiovascular, neurological, psychiatric diseases and severe visual/auditory impairments; absence of musculoskeletal pathologies influencing locomotion, with the exception of stroke; ability to stand up from a chair, walk along 6m and sit down (TUG); resistance to fatigue allowing to walk for two minutes; ability to understand and follow instructions.

The Review Board Committee of the authors' institution approved the study, and informed consent was obtained from all participants.

5.3.2 Clinical evaluation

In agreement with clinicians, a selection of clinical scales was implemented in order to obtain a complete ICF description of stroke outcomes.
The selected clinical scales were:

a) Motricity Index (MI): to assess limb motor function.
b) Trunk Control Test (TCT): to evaluate trunk control.
c) Rivermead Mobility Index (RMI): to assess different aspects of mobility in everyday life situations.
d) Functional Ambulation Category (FAC): to evaluate patient's walking ability.

e) Walking Handicap Scale (WHS): to evaluate the actual use of walking in daily life.
f) Cumulative Illness Rating Scale (CIRS): to measure the patient's somatic health. It comprises Severity Index (SI) and Co-morbidity Index (CI).

Each subject also performed two clinical motor tests:

a) 2MWT: endurance test that measures the travelled distance (d_2MWT) in 2 minutes of walking at self-selected speed in a corridor longer than 80 m.
b) TUG: a simple test to measure mobility level as well as static and dynamic balance skills. It consists of rising from a chair, walking 6 m, turning around, walking back to the chair and siting down. The clinical outcome is the test execution time (t_TUG).

The same expert clinician performed all assessments to avoid inter-evaluator errors.

5.3.3 Experimental setup

One 3D-accelerometer (G-Walk, BTS Bioengineering, Italy; f_s = 200Hz) was mounted on the lower trunk as close as possible to L5 to record approximately the acceleration of the centre of mass.

5.3.4 Data analysis

The whole signal of 2MWT and the walking portions [17] of TUG were used for the calculation of stability indexes.

Among all the indexes proposed in the literature for the quantification of gait stability [11,19], Sample Entropy (SEN) [20] and Recurrence Quantification Analysis (RQA) in particular the analysed features were: recurrence rate (RR), determinism (DET) and averaged diagonal line length (AvgL) [21–23], were chosen (see Chapter 1 for computational details), because they did not require step segmentation [11], which can be critical in stroke patients due to the alteration of gait cycle; moreover these indexes could be quantified with acceptable reliability

[19] for the limited duration of the walking section of TUG. For all the computational details see Chapter 1.

All indexes were calculated for the antero-posterior (AP), medio-lateral (ML) and vertical (V) trunk acceleration direction.

Jarque-Bera test was performed to verify the normal distribution of the calculated indexes on the different groups (i.e. TUG, 2MWT, *NoCane*, *Cane*): since the normal distribution was not verified for all groups, median, 25- and 75-percentile values were calculated.

Kruskal-Wallis test with minimum level of significance at 5% was used to perform the paired comparison of the effect of TUG vs 2MWT and of *NoCane* vs *Cane* on SEN for all time scales and all RQA features in each direction. Pearson correlation coefficients and the associated *p_value* were calculated per group (i.e. *NoCane* and *Cane*) and per task (i.e. TUG and 2MWT) between the log-transform of the indexes and the scores of clinical scales.

5.4 RESULTS

For SEN:

- SENap and SENv showed higher values for all time scales during TUG than during 2MWT, in both *NoCane* and *Cane* group. In ML direction the opposite trend was found.
- *NoCane* and *Cane* groups showed similar values of SENap obtained for 2MWT; whereas, during the execution of TUG: *NoCane* had lower median values than *Cane* for τ=1,2 and opposite trend for τ ranging from 3 to 6.
- SENv, calculated for 2MWT, showed lower values for *NoCane* subjects than for *Cane* ones for τ=1,2 and the opposite trend was found with τ ranging form 3 to 6.

- For TUG instead, *NoCane* showed values lower than *Cane* with τ ranging from 1 to 5, and the opposite trend for τ=6.
- SENml showed higher values for *NoCane* than for *Cane* in both tasks.
- Kruskal-Wallis test on SENml (τ=1,2) showed a significant task effect for the *NoCane* group (p=0.01 and p=0.03), while SENv (τ=1,2) showed a significant supports effect during the execution of TUG (p=0.002 and p=0.04).

For RQA:

- DET and AvgL, in all directions, showed opposite trends both for groups and tasks. In particular: DET calculated for 2MWT showed higher values than for TUG. Moreover, DET showed higher values for *NoCane* subjects than for *Cane* ones.
- Kruskal-Wallis test showed support (*NoCane* vs *Cane*) effect on RRml (p=0.009), DETv (p=0.002) and in all directions for AvgL (p<0.05) if calculated on 2MWT, while for RRap and DETv (p=0.01) if calculated on TUG data. Task effect was found for *NoCane* group on RR, DET and AvgL in AP and ML directions (p<0.04), while on RR and DET in V direction (p=0.03) for *Cane* subjects.

Median values, 25^{th} and 75^{th} percentiles of SEN (for all τ) and RQA (all features) are shown in Figure 1 and 2, respectively.

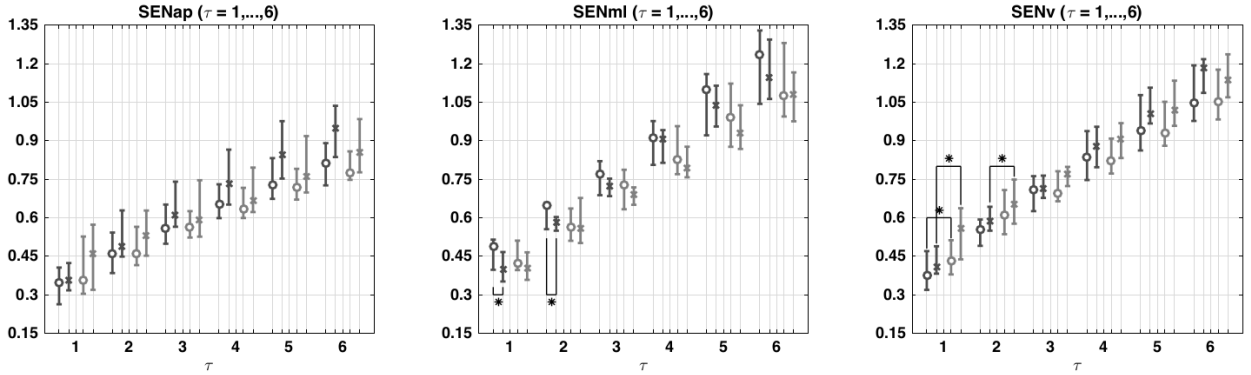

Figure 1. Median values (and 25th and 75th percentiles) for SEN values. Groups are identified by color (*NoCane* light grey and *Cane* dark grey) and tasks by symbol (of median values) (o for 2MWT and x for TUG). Asterisks (*) represent statistically significant differences (p_value<5%) between: tasks (same group), if above the bar plot, or groups (same task) if under the bar-plots.

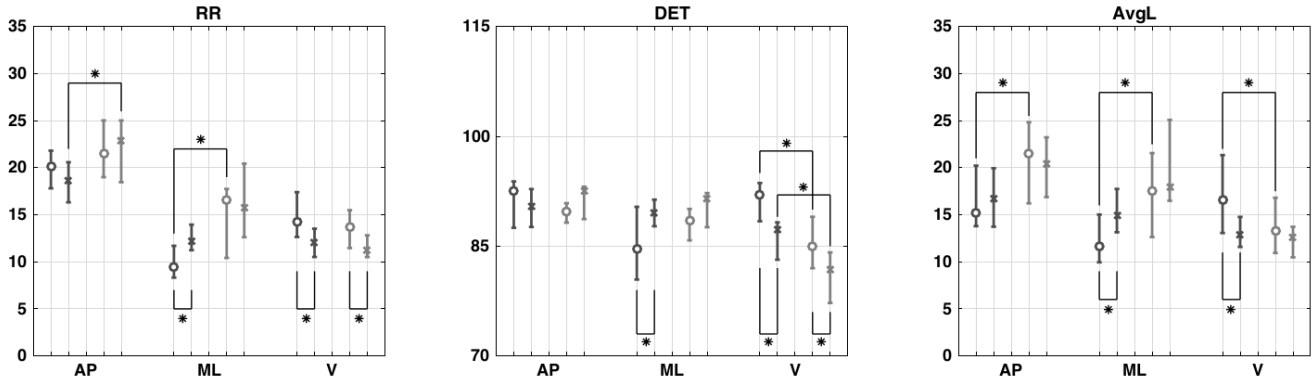

Figure 2. Median values (and 25th and 75th percentiles) for RR, DET and AvgL values. Groups are identified by color (*NoCane* light grey and *Cane* dark grey) and tasks by symbol (of median values) (o for 2MWT and x for TUG). Asterisks (*) represent statistically significant differences (p_value<5%) between: tasks (same group) if above the bar plot, or groups (same task) if under the bar-plot.

Regarding the correlation of indexes with clinical rating scales, in *NoCane* group:

- for both tasks, SENap and RQAap (all features) correlated significantly with WHS; moreover, RQAml (all features) correlated with t_TUG, d_2MWT and MI, while RQAv (all features) showed no correlation.
- SENml (τ=2,3) correlated with WHS, during the execution of 2MWT, and with t_TUG (τ=2…6) and d_2MWT (τ=2…4) during TUG.
- SENv (τ=2…6), calculated for 2MWT, correlated with t_TUG.
- No correlation was found for RQAv with clinical scales in both conditions.

In *Cane* Group:

- for both tasks, RQAap correlated with t_TUG and SENap showed no correlation
- SENml (τ=5,6), calculated on TUG, correlated with FAC.

Pearson correlation coefficients (*p_value* lower than 5%) between the indexes from the two tasks and the clinical scores are reported in Table 1 and Table 2 for *NoCane* and *Cane* group, respectively.

INDEXES		CLINICAL SCALES								
		t_TUG	MI	TCT	RMI	d_2MWT	FAC	WHS	SI	CI
SEN_ap1	2MWT				-0,48			-0,59		
	TUG	0,55				-0,63		-0,64		
SEN_ap2	2MWT							-0,59		
	TUG							-0,67		
SEN_ap3	2MWT							-0,55		
	TUG							-0,64		
SEN_ap4	2MWT							-0,58		
	TUG							-0,65		
SEN_ap5	2MWT							-0,53		
	TUG							-0,59		
SEN_ap6	2MWT							-0,52		
	TUG							-0,59		
SEN_ml1	2MWT									
	TUG									
SEN_ml2	2MWT									
	TUG	-0,69				0,57				

INDEXES		CLINICAL SCALES								
		t_TUG	MI	TCT	RMI	d_2MWT	FAC	WHS	SI	CI
SEN_ml3	2MWT							-0,50		
	TUG	-0,56				0,58				
SEN_ml4	2MWT							-0,48		
	TUG	-0,49				0,50				
SEN_ml5	2MWT									
	TUG	-0,48								
SEN_ml6	2MWT									
	TUG	-0,50								
SEN_v1	2MWT			-0,53						
	TUG									
SEN_v2	2MWT	-0,53								
	TUG									
SEN_v3	2MWT	-0,54								
	TUG									
SEN_v4	2MWT	-0,55								
	TUG									
SEN_v5	2MWT	-0,57								
	TUG									
SEN_v6	2MWT	-0,52								
	TUG									
RR_ap	2MWT									
	TUG							0,55		
DET_ap	2MWT							0,51		
	TUG				0,72		0,69	0,89		
AVG_ap	2MWT							0,58		
	TUG							0,67		
RR_ml	2MWT	0,68				-0,63				
	TUG	0,84				-0,68				
DET_ml	2MWT	0,49	-0,49			-0,55				
	TUG	0,67	-0,48			-0,63				
AVG_ml	2MWT	0,66				-0,63				
	TUG	0,75	-0,58			-0,64				

Table 1. Significant Pearson correlation coefficients (*p_value*<5%) of *NoCane* subjects. White lines: (significant) correlations between indexes, obtained from 2MWT, and clinical scales. Grey lines: (significant) correlations between indexes, obtained from TUG, and clinical scales.

INDEXES		CLINICAL SCALES								
		t_TUG	MI	TCT	RMI	d_2MWT	FAC	WHS	SI	CI
SEN_ml1	2MWT									0,42
	TUG									
SEN_ml2	2MWT									
	TUG									
SEN_ml3	2MWT									
	TUG									
SEN_ml4	2MWT									
	TUG									

INDEXES		CLINICAL SCALES								
		t_TUG	MI	TCT	RMI	d_2MWT	FAC	WHS	SI	CI
SEN_ml5	2MWT									
	TUG						-0,55			
SEN_ml6	2MWT									
	TUG						-0,63			
SEN_v1	2MWT					-0,61				
	TUG	0,56						-0,64		
SEN_v2	2MWT					-0,63				
	TUG							-0,65		
SEN_v3	2MWT					-0,58				
	TUG							-0,56		
RR_ap	2MWT									
	TUG					-0,57	-0,55			
DET_ap	2MWT									
	TUG					-0,54				
AVG_ap	2MWT									
	TUG									
RR_ml	2MWT	0,69						-0,57		
	TUG	0,72								
DET_ml	2MWT	0,55						-0,62		
	TUG	0,57								
AVG_ml	2MWT	0,55								
	TUG	0,67								

Table 2. Significant Pearson correlation coefficients (*p_value*<5%) of *Cane* subjects. White lines: (significant) correlations between indexes, obtained from 2MWT, and clinical scales. Grey lines: (significant) correlations between indexes, obtained from TUG, and clinical scales.

5.5 DISCUSSION

To analyse how stability indexes are affected by specific experimental conditions and correlate with all clinical rating scales, SEN and RQA were calculated for trunk acceleration data collected during 2MWT and TUG in two groups of sub-acute stroke subjects (*NoCane* and *Cane*). The same subjects were also assessed with clinical rating scales by the same expert evaluator.

Both SEN and RQA have been proposed as metrics for the quantification of motor stability, although they actually quantify different specific characteristics

of the analysed signal. From the perspective of its mathematical implementation, SEN is a conditional probability measure that quantifies the likelihood of a sequence of m consecutive data points, matching another sequence of the same length, to still match the other sequence when their length is increased of one sample [24]. SEN provides a measure of unpredictability or irregularity of the time series that should not be always interpreted as complexity: a very periodic signal and a highly random one are both very low in complexity, but have different SEN values [25]. However, for the sake of the present study, SEN can be considered a measure of how much the acquired trunk acceleration deviates from the cyclic nature of gait and, therefore, in this context it is common practice to interpret SEN as a measure of complexity [20,24,26].

Comparing SEN values, obtained for the two tasks in both groups, they were found higher during 2MWT than during TUG in both AP and V directions, while the opposite trend was observed in ML direction. TUG can be considered to require higher cognitive (i.e. programming the next movement) and biomechanical (i.e. adapting gait pattern to the task constrains) efforts than 2MWT to correctly complete the task. In this perspective, these results are in agreement with those previously reported by Lamoth et al. [27], who reported higher values of SEN in AP direction, but not in ML (V was not analysed), analysing elderly subjects performing dual task, and interpreted this result as an indicator that changes in cognitive functions result in changes in gait complexity and automaticity. Accordingly, these results suggest that gait during 2MWT is perceived as less complex/more automatic than that during TUG.

The support effect on SEN was found mainly in V direction and for low τ values. Even if the results were not all statistically significant, a trend could be observed: in ML direction, for both tasks, *NoCane* subjects showed higher SEN values than *Cane* ones. SEN results can be related to the level of automaticity in the control of gait, therefore small SEN values can be associated to high automaticity [26]. In this perspective, these results suggest that *NoCane* subjects exhibit a more complex (less automatic) gait pattern than *Cane* ones in ML direction, highlighting the dominant constraint of the cane in this direction.

In AP and V directions, SEN changes for increasing τ. For τ from 1 to 3, *Cane* subjects showed higher SEN than *NoCane* ones, *vice versa* for higher τ. τ values lower than 3 (i.e. frequency components higher than 33Hz) were characterized by high complexity for *Cane* subjects, while τ higher than 4 (namely frequency below 25Hz) for *NoCane* ones. In general, this suggests that *Cane* subjects are characterized by high complexity at high frequencies (low τ), *vice versa* for *NoCane* ones. This could be explained taking into account muscular stiffness, a characteristic symptom of stroke patient, magnified by the use of supports.

From the perspective of their mathematical implementation, RQA features quantify the structure in the recurrence plot. In particular, DET relates to how often the trajectory re-visits similar state space locations ("shape"), the higher DET the more regular is the dynamic structure of the data [28]; AvgL is the average length of all the found diagonal structures [11,28] (i.e. how long the repeated trajectory 'lasts'), this can be interpreted as the duration of the most repeated "shape". It is related to the velocity in the execution of the test (i.e. higher AvgL is expected for slower gait), but this duration is not independent from the regularity of the pattern (i.e. the gait is slower because each stride on average is slower). Therefore, results suggest that: i) all groups had a more regular dynamic structure of gait during 2MWT than during TUG, confirming TUG gait more challenging/less automatic; ii) *NoCane* group repeated the same "shapes" more than *Cane*, in agreement with Labini et al. [21]. On the other hand, AvgL results can be explained by its intrinsic time dependent nature: *NoCane* subjects were, in general, faster than *Cane* ones, thus *NoCane* repeated shapes were shorter than *Cane* ones. Moreover, during 2MWT all subjects walked faster than during TUG, thus the repeated trajectories were shorter in TUG than in 2MWT.

To the knowledge of the authors, the correlation between stability indexes and the scores of clinical scales in sub-acute stroke subjects was not assessed previously.

In *NoCane*, WHS correlated positively with RQAap and negatively with SENap in both tasks, this suggests that subjects with a good use of walking in daily life

exhibit slow gait pattern (i.e. high AvgL), high regularity (i.e. high RR and DET), and low complexity/high automaticity (i.e. low SEN) [26] of gait in AP direction.

High regularity (i.e. high RR and DET) and a slow pattern (i.e. high AvgL) in AP direction also correlated positively with t_TUG, commonly associated to low functional performance, but in these subjects correlated positively with WHS, due to the concurrent high regularity (i.e. high RR and DET), and low complexity/high automaticity (i.e. low SEN) of the gait pattern. Moreover, SENml and SENv also correlated negatively with t_TUG. This result confirms that a gait pattern with an increased t_TUG, but regular and slow in AP direction and with low complexity/high automaticity in AP, and ML or V directions, although slow is similar to that of an healthy subject [21,26,29], still providing a good functional outcome (i.e. higher WHS values). This seems to suggest that TUG outcomes could be analysed and interpreted in more detail using non-linear indexes, and related to other functional scales, providing insight in the actual effective use of gait in daily life.

The negative correlation between WHS and SENv for *Cane* and *NoCane* subjects confirms an efficient walking related to low complexity/high automaticity, and seems suggests that the use of the cane constraints the gait pattern not only in ML but also AP direction.

As for *NoCane*, t_TUG correlates positively with RQAml also in *Cane*, supporting the idea that a high t_TUG is not necessarily related to a reduced gait performance, and a decreased speed can still be associated to a functional gait pattern in daily life.

Of course, these results require further investigation, due to the very specific analysed population and the limited number of subjects, which could be a possible limitation of the study. Nevertheless, the coherence of the results of the statistics in the different conditions, and the accordance with existing literature, support these preliminary results for future investigations.

No correlation was found with CIRS, but, considering the specific population analysed in the present study, this is not surprising, since stroke outcome is likely to be predominant over all other possible pathologies. Minor, but promising, correlations were found between RQAml and MI and between

SENml and FAC, suggesting that RQAml and SENml could identify changes in motor abilities in limbs and in walking, respectively. Nevertheless, these results require further investigations, due to the small number of subjects analysed and to the moderate and sparse values of the obtained Pearson coefficient.

One possible limitation, of this preliminary study, is the limited number strides (few more than 10) in the analysed gait section for TUG. Nevertheless, Riva et al. [19] showed that 10 strides are sufficient to reach a steady value and reliability is quite high (at least 20%) for SEN and RQA. Moreover, time series from TUG included a number of data points between 2800 and 8000, and SEN is largely independent on the time series length when the total number of data points is larger than 750 [20,30].

In conclusion, this preliminary study suggest that: i) both complexity (SEN) and repeatability (RQA) of gait pattern are influenced by the use of supports in ML direction; ii) TUG gait is a more challenging than 2MWT; iii) non-linear stability indexes SEN and RQA show promising correlations with clinical scales, potentially providing a better insight in the functional analysis of gait pattern. In particular, a regular (i.e. high RR and DET) gait pattern with low complexity (i.e. low SEN) and slow pattern (i.e. high AvgL) in AP direction can be related to an efficient use of walking in daily life (WHS), although an overall slow speed associated to high values of t_TUG.

Clearly, for an effective exploitation in clinical practice, further efforts are required to establish reference values for indexes and correlated clinical scales. Future researches will focus on the inclusion of a higher number of participants per group and on the assessment of different populations. These improvements will allow to strengthen and to further understand these preliminary conclusions.

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5.7 REFERENCES

[1] B. Homann, A. Plaschg, M. Grundner, A. Haubenhofer, T. Griedl, G. Ivanic, E. Hofer, F. Fazekas, C.N. Homann, The impact of neurological disorders on the risk for falls in the community dwelling elderly: a case-controlled study, BMJ Open. 3 (2013). doi:10.1136/bmjopen-2013-003367.

[2] Z. Sawacha, E. Carraro, P. Contessa, A. Guiotto, S. Masiero, C. Cobelli, Relationship between clinical and instrumental balance assessments in chronic post-stroke hemiparesis subjects, J. NeuroEngineering Rehabil. 10 (2013) 95. doi:10.1186/1743-0003-10-95.

[3] K.J. Sullivan, On "Modified constraint-induced therapy…" Page and Levine. Phys Ther. 2007;87:872–878., Phys. Ther. 87 (2007) 1560–1560. doi:10.2522/ptj.2007.87.11.1560.

[4] N.H. Mayer, A. Esquenazi, Muscle overactivity and movement dysfunction in the upper motoneuron syndrome, Phys. Med. Rehabil. Clin. N. Am. 14 (2003) 855–883, vii–viii.

[5] A.B. Ward, A literature review of the pathophysiology and onset of post-stroke spasticity, Eur. J. Neurol. 19 (2012) 21–27. doi:10.1111/j.1468-1331.2011.03448.x.

[6] H.-C. Huang, K.-C. Chung, D.-C. Lai, S.-F. Sung, The impact of timing and dose of rehabilitation delivery on functional recovery of stroke patients, J. Chin. Med. Assoc. JCMA. 72 (2009) 257–264. doi:10.1016/S1726-4901(09)70066-8.

[7] S.H. Peurala, A.H. Karttunen, T. Sjögren, J. Paltamaa, A. Heinonen, Evidence for the effectiveness of walking training on walking and self-care after stroke: a systematic review and meta-analysis of randomized controlled trials, J. Rehabil. Med. 46 (2014) 387–399. doi:10.2340/16501977-1805.

[8] D. Hamacher, N.B. Singh, J.H. Van Dieën, M.O. Heller, W.R. Taylor, Kinematic measures for assessing gait stability in elderly individuals: a systematic review, J. R. Soc. Interface. 8 (2011) 1682–1698. doi:10.1098/rsif.2011.0416.

[9] J.D. O'Sullivan, C.M. Said, L.C. Dillon, M. Hoffman, A.J. Hughes, Gait analysis in patients with Parkinson's disease and motor fluctuations: Influence of levodopa and comparison with other measures of motor function, Mov. Disord. 13 (1998) 900–906. doi:10.1002/mds.870130607.

[10] S. Gillain, E. Warzee, F. Lekeu, V. Wojtasik, D. Maquet, J.-L. Croisier, E. Salmon, J. Petermans, The value of instrumental gait analysis in elderly healthy, MCI or Alzheimer's disease subjects and a comparison with other clinical tests used in single and dual-task conditions, Ann. Phys. Rehabil. Med. 52 (2009) 453–474. doi:10.1016/j.rehab.2008.10.004.

[11] F. Riva, M.J.P. Toebes, M. Pijnappels, R. Stagni, J.H. van Dieën, Estimating fall risk with inertial sensors using gait stability measures that do not require step detection, Gait Posture. 38 (2013) 170–174. doi:10.1016/j.gaitpost.2013.05.002.

[12] F. Riva, M.C. Bisi, R. Stagni, Orbital stability analysis in biomechanics: A systematic review of a non-linear technique to detect instability of motor tasks, Gait Posture. 37 (2013) 1–11. doi:10.1016/j.gaitpost.2012.06.015.

[13] H.B. Menz, S.R. Lord, R.C. Fitzpatrick, Acceleration patterns of the head and pelvis when walking on level and irregular surfaces, Gait Posture. 18 (2003) 35–46. doi:10.1016/S0966-6362(02)00159-5.

[14] M. Kosak, T. Smith, Comparison of the 2-, 6-, and 12-minute walk tests in patients with stroke, J. Rehabil. Res. Dev. 41 (2004) 103. doi:10.1682/JRRD.2003.11.0171.

[15] K.E. Light, A.L. Behrman, M. Thigpen, W.J. Triggs, The 2-Minute Walk Test: A Tool for Evaluating Walking Endurance in Clients with Parkinson's Disease., J Neurol Phys Ther. 21 (1997) 136–139.

[16] A. Weiss, T. Herman, M. Plotnik, M. Brozgol, I. Maidan, N. Giladi, T. Gurevich, J.M. Hausdorff, Can an accelerometer enhance the utility of the Timed Up & Go Test when evaluating patients with Parkinson's disease?, Med. Eng. Phys. 32 (2010) 119–125. doi:10.1016/j.medengphy.2009.10.015.

[17] L. Palmerini, S. Mellone, G. Avanzolini, F. Valzania, L. Chiari, Quantification of Motor Impairment in Parkinson's Disease Using an Instrumented Timed Up and Go Test, IEEE Trans. Neural Syst. Rehabil. Eng. 21 (2013) 664–673. doi:10.1109/TNSRE.2012.2236577.
[18] A.L. Leddy, B.E. Crowner, G.M. Earhart, Utility of the Mini-BESTest, BESTest, and BESTest Sections for Balance Assessments in Individuals with Parkinson Disease, J. Neurol. Phys. Ther. JNPT. 35 (2011) 90–97. doi:10.1097/NPT.0b013e31821a620c.
[19] F. Riva, M.C. Bisi, R. Stagni, Gait variability and stability measures: Minimum number of strides and within-session reliability, Comput. Biol. Med. 50 (2014) 9–13. doi:10.1016/j.compbiomed.2014.04.001.
[20] M. Costa, C.-K. Peng, A. L. Goldberger, J.M. Hausdorff, Multiscale entropy analysis of human gait dynamics, Phys. Stat. Mech. Its Appl. 330 (2003) 53–60. doi:10.1016/j.physa.2003.08.022.
[21] F. Sylos Labini, A. Meli, Y.P. Ivanenko, D. Tufarelli, Recurrence quantification analysis of gait in normal and hypovestibular subjects, Gait Posture. 35 (2012) 48–55. doi:10.1016/j.gaitpost.2011.08.004.
[22] M.A. Riley, R. Balasubramaniam, M.T. Turvey, Recurrence quantification analysis of postural fluctuations, Gait Posture. 9 (1999) 65–78. doi:10.1016/S0966-6362(98)00044-7.
[23] C.L. Webber, J.P. Zbilut, Dynamical assessment of physiological systems and states using recurrence plot strategies, J. Appl. Physiol. Bethesda Md 1985. 76 (1994) 965–973.
[24] J.S. Richman, J.R. Moorman, Physiological time-series analysis using approximate entropy and sample entropy, Am. J. Physiol. - Heart Circ. Physiol. 278 (2000) H2039–H2049.
[25] N. Stergiou, Non-linear Analysis for Human Movement Variability, CRC Press, 2016.
[26] M.C. Bisi, R. Stagni, Complexity of human gait pattern at different ages assessed using multiscale entropy: From development to decline, Gait Posture. 47 (2016) 37–42. doi:10.1016/j.gaitpost.2016.04.001.
[27] C.J. Lamoth, F.J. van Deudekom, J.P. van Campen, B.A. Appels, O.J. de Vries, M. Pijnappels, Gait stability and variability measures show effects of impaired cognition and dual tasking in frail people, J. Neuroengineering Rehabil. 8 (2011) 2. doi:10.1186/1743-0003-8-2.
[28] C.L. Webber, J.P. Zbilut, Dynamical assessment of physiological systems and states using recurrence plot strategies, J. Appl. Physiol. 76 (1994) 965–973.
[29] M.C. Bisi, F. Riva, R. Stagni, Measures of gait stability: performance on adults and toddlers at the beginning of independent walking, J. NeuroEngineering Rehabil. 11 (2014). doi:10.1186/1743-0003-11-131.
[30] J.M. Yentes, N. Hunt, K.K. Schmid, J.P. Kaipust, D. McGrath, N. Stergiou, The Appropriate Use of Approximate Entropy and Sample Entropy with Short Data Sets, Ann. Biomed. Eng. 41 (2013) 349–365. doi:10.1007/s10439-012-0668-3.

CONCLUSION

"We are made wise not by the recollection of our past,
but by the responsibility for our future."
George Bernard Shaw

The purpose of this dissertation was to improve the understanding of the non-linear metrics proposed for the quantification of locomotor stability, contributing to the identification of methodological references for their implementation and experimental assessment, and suggesting a possible clinical interpretation in a specific clinical context.

These non-linear metrics originated from dynamical system theory (e.g. Lyapunov Exponents [9], Recurrence Quantification Analysis [10], and Poincaré Plots features [11]), frequency domain analysis (e.g. Harmonic Ratio [12], Index of Harmonicity [13]), and information theory (e.g. Sample Entropy). They quantify different signal features, aiming to identify underlying system characteristics. An illustration of the mathematical reference of the analysed metrics, highlighting the role of relevant parameters and the possible interpretation when applied in gait analysis, was given in Chapter 1.

Relevant open issues have been addressed in this thesis (Chapter 2, 3 and 4) about the definition of methodological references for the implementation and experimental assessment of the analysed non-linear metrics.

First of all, in order to provide indications for the proper signal acquisition and processing, the spectrum of lower trunk acceleration signal during gait was characterized as related to age in different populations (i.e. 7, 9, 15, 25, 45, 65, and 85 years of age). The harmonic content (at 98% of the normalized power) of the trunk acceleration signal for all the analysed age groups, with exception of the

adolescents, resulted below 30 Hz, with the high frequency contribution in the antero-posterior direction. In the adolescent population, spectrum amplitude reached 45 Hz. This result allowed to define a standard reference for sampling frequency of gait trunk acceleration: sampling frequency higher than 60 Hz (90 Hz for the adolescents) is necessary to avoid aliasing effect and to not lose signal information.

These results are directly related with the study presented in Chapter 3, which aims to evaluate the effect of sampling frequency down-scaling on non-linear index estimation. Smartphones with embedded accelerometers can been considered ideal devices for continuous monitoring; if, on one hand, their advantages are clear (on board inertial sensors, user-friendliness, low cost, etc.), on the other hand, they hardly support data acquisition from on board sensor with sampling frequency higher than 50 Hz. Consequently, it comes clear the importance of evaluating the effect of sampling frequency down-scaling on indexes estimation. The results suggest that indexes analysing the frequency content of the signal are not influenced by sampling frequency reduction (down to 42 Hz), while those analysing signal in the time domain are. However, by using appropriate interpolation methods, this issue can be overcome.

Other relevant aspects that can influence gait assessment, in particular when using non-linear metrics, are testing environment and walking condition protocol. Aiming to evaluate these, the walking pattern of young healthy adults (control/referred population) was analysed in different environments (indoor and outdoor) and testing conditions (controlled and free) to assess if and how gait variability and stability, quantified using non-linear metrics, would be affected. The hypothesis in the specific population was that stability would not change significantly, variability *vice versa*. The results confirmed, in general, the ability of the analysed metrics to quantify the target characteristics of gait, although with different levels of accuracy, and in particular, that metrics for the quantification of stability and variability do actually different aspects of motor control and are affected in different ways by experimental conditions.

Finally, in the last Chapter (Chapter 5) of this Thesis, the possible clinical interpretation of the proposed metrics was investigated. The relationship between

the non-linear metrics, instrumental gait characterization, and an extended selection of clinical rating scales (standard clinical gait assessment) was evaluated in a sub-acute stroke population. The study suggests that non-linear stability indexes (i.e. Sample Entropy and Recurrence Quantification Analysis) show promising correlations with clinical scales, and potentially provide a better insight in the functional analysis of gait pattern.

Even though not exhaustive, these results provide essential basic knowledge for the definition of a reference for the reliable use and interpretation of the analysed non-linear metrics. Future natural development will be extending the same investigations to different, both healthy and pathological, populations, in order to overcome the main limitations of this dissertation, namely the possibility to generalize (when and if possible) the obtained results to other populations.

In conclusion, this Thesis provides relevant and clear guidelines for a correct and reliable implementation and experimental assessment of the analysed non-linear indexes; moreover they lay the groundwork for a better insight of the clinical functional correlation of the non-linear indexes.

The obtained results will allow, henceforth, to perform the assessment of gait stability without bias due to the different experimental conditions and absence of an implementation methodology reference.

"The important thing is not to stop questioning.
Curiosity has its own reason for existing."
Albert Einstein

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