EPFL

Thèse n° 7687

Gait analysis in children with cerebral palsy: bridging the gap between the laboratory and real life

Présentée le 2 octobre 2020

à la Faculté des sciences et techniques de l'ingénieur
Laboratoire de mesure et d'analyse des mouvements
Programme doctoral en biotechnologie et génie biologique

pour l'obtention du grade de Docteur ès Sciences

par

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École polytechnique fédérale de Lausanne

2020

Da ma familh muiañ karet

Acknowledgements/Remerciements

Tout d'abord je souhaite remercier mes deux directeurs de thèse, Prof. Kamiar Aminian de l'EPFL et Dr. Stéphane Armand de l'Université de Genève. Je vous remercie Kamiar pour avoir rendu possible mon intégration à l'EPFL, et pour m'avoir donné l'opportunité d'intégrer pleinement votre équipe du LMAM malgré le travail à distance depuis Genève. Je vous remercie également pour votre suivi tout au long de mon doctorat qui m'a permis d'avancer avec sérénité. Je te remercie Stéphane pour l'inconditionnelle confiance que tu m'as accordée depuis le début de notre collaboration. C'est grâce à toi que j'ai pu réaliser cette thèse sur un sujet qui m'a passionné du début à la fin. Merci d'avoir été disponible, à l'écoute à tout moment, d'avoir suivi mon travail si rigoureusement et m'avoir toujours donné de précieux conseils scientifiques desquels j'ai beaucoup appris. Et merci aussi pour ton soutien et tes encouragements dans les moments difficiles rencontrés durant cette thèse.

En second lieu, je souhaite remercier Dr. Christopher Newman du Centre Hospitalier Universitaire Vaudois (CHUV) qui a non-officiellement endossé le rôle de troisième directeur de thèse. Christopher était à l'initiative du projet principal intégré dans ce travail doctoral. Il m'a suivi tout au long de mon doctorat en m'apportant de précieux conseils tant sur le plan clinique que sur le plan méthodologique. Christopher m'a également fait confiance au point de me proposer un poste dans son équipe de recherche au moment où mes financements de thèse se terminaient. Encore merci Christopher, je t'en suis très reconnaissante.

Ensuite, je remercie très chaleureusement Dr. Geraldo De Coulon des Hôpitaux Universitaires de Genève (HUG), qui a su me transmettre sa passion pour l'analyse clinique de la marche. Nos discussions, au cours des séances d'interprétations de cas cliniques notamment, m'ont guidées tout au long de ce doctorat et ont largement contribuées à donner du sens à mon travail.

Je remercie également Dr. Joel Fluss des HUG, qui m'a fait découvrir le volet cognitif de l'analyse de la marche. Merci Joel pour ta confiance, ton suivi et ta disponibilité au cours de notre projet.

Je tiens bien-sûr à remercier mes divers collaborateurs et co-auteurs d'articles. Je remercie Dr. Corinna Gerber du CHUV avec qui j'ai travaillé main dans la main pendant tout ce doctorat. Merci Corinna pour ta disponibilité inconditionnelle, que ça soit pour venir m'aider dans la collecte des données les soirs et samedi matins, pour répondre à chacune de mes interrogations ou pour tes commentaires toujours très pertinents et construits lors de tes relectures. Je remercie Dr. Anisoara Paraschiv-Ionescu de l'EPFL pour m'avoir supervisé conjointement avec le Prof. Kamiar Aminian du début à la fin de ce doctorat. Je te remercie pour tes conseils techniques et méthodologiques. Merci d'avoir pris le temps de m'expliquer les concepts nouveaux abordés durant ma thèse. Je remercie ensuite Dr. Gilles Allali et Mme Nathalie Valenza des HUG pour leurs disponibilités et leurs remarques très pertinentes ayant permis d'ajouter une plus-value clinique à mon travail.

Je remercie les membres de mon jury, Prof. Claudia Mazza, Prof. Sylvain Brochard et Prof. Grégoire Courtine, examinateurs de cette thèse, et Prof. Auke Isjpeert, président du jury. Merci d'avoir accepté d'évaluer mon travail, et merci pour les questions et commentaires très pertinents lors de mon examen oral.

Je souhaite remercier également l'équipe de GaitUp, notamment Rebekka Anker, Stéphane Lovejoy et Benoît Mariani qui m'ont aidé dans la prise en main des Physilog, ont toujours répondu à mes appels à l'aide et m'ont apporté des conseils sur la manipulation des capteurs mais également le traitement des données.

Ce travail de thèse n'aurait été possible sans le soutien financier de diverses fondations. Je remercie donc la Fondation Leenaards (Lausanne, Suisse), la Fondation Paralysie Cérébrale (Paris, France), la Fondation

Science for Smiles (Villeneuve, Suisse), la Fondation de Recherche Orthopédique de Lausanne (Lausanne, Suisse) ainsi que les HUG (Genève, Suisse) via le programme « Projets de Recherche et Développement ».

Ce doctorat n'aurait pas non plus vu le jour sans la participation des 60 enfants et adolescents qui ont accepté de passer plusieurs heures avec moi au laboratoire de marche, parfois de revenir à une semaine d'intervalle et parfois même de m'avoir accepté chez eux enfin que je les forme à l'utilisation des capteurs. Un grand merci à eux et à leurs parents !

Je remercie ensuite les 3 équipes de recherche qui m'ont accueilli durant ce doctorat :

En premier lieu, je remercie mes collègues et amis du laboratoire de cinésiologie Willy Taillard qui ont très largement contribué au plaisir que j'avais de venir travailler chaque matin (sans exception). Les membres de cette famille Cinésio ont toujours été présents tant pour m'épauler sur des sujets scientifiques que pour me changer les idées autour d'un verre, d'une piste d'athlétisme ou d'un écran de télévision en période de JO d'hivers. Merci Anne, Kevin, Alice, Michael, Xavier, Magali, Jennifer, Mickael, Annie, Florent, ainsi que toutes les personnes ayant fait un passage plus court au laboratoire, Léonie, Anaïs, Sophie, Léopoldine, Honoré, Antoine, Sébastien et Samuel.

Ensuite, je souhaite sincèrement remercier les membres du LMAM qui m'ont accueilli comme si j'étais un membre à plein temps de leur équipe. Merci Pritish, Matthieu, Matteo, Chris, Benedikt, Pascal, Francine, Abolfazl, Arash, Gaëlle, Salil, Mahdi, Wei, Hooman, Mina, Yasaman et tous les étudiants qui sont passé par le LMAM. Merci pour l'astmosphère bienveillante et sympa que vous apportez au labo et pour les discussions scientifiques qui m'ont beaucoup aidé dans ce travail doctoral.

Enfin, je remercie la petite équipe de recherche de l'unité de neurologie et neuroréhabilitation pédiatrique du CHUV constitué de Corinna, Thomas, Didier et Manon. Merci à vous pour votre aide dans la récolte des données et pour votre enthousiasme dans les projets que vous avez menés. Et merci aussi à tous les collègues de l'unité qui m'ont accueilli chaleureusement à chacune de mes visites.

J'ai également réussi à accomplir ce travail de thèse grâce aux nombreux moments d'évasion proposés par mes amis du swing, de l'UTC, de Paris, de Bretagne et partout ailleurs. Impossible de tous les citer ici, c'est bien dommage. Merci à vous qui vous reconnaitrez.

Merci aussi à ma belle-famille, notamment Isabelle, Florence et Thibaut, qui m'a beaucoup soutenu et m'a aider à décompresser durant les weekends.

Je remercie toute ma famille, en particulier mes parents, Ewen, Gwenal, Gaëlle et Patricia, pour son soutien à distance et ses encouragements tout au long de mon travail. Il n'a pas toujours été facile d'être loin de vous. Merci aussi d'être venu me rendre visite. Sans oublier Maden, Anna et Bleuenn, qui m'ont bien aidé à me ressourcer.

Et pour finir, je remercie du fond du cœur Charles pour avoir supporté le meilleur et le pire durant ces 4 années de thèse. Tu as constamment été avec moi, même à distance, pour m'encourager, me remonter le moral et m'aider à relativiser dans les moments difficiles. Merci aussi pour tes précieux conseils et relectures durant la préparation de ce manuscrit et de la soutenance qui m'ont aidé à prendre confiance en moi. A nous le début d'une vie vraiment ensemble maintenant !

Lena Carcreff, le 21 Décembre 2019

Preamble

In the biomedical field, scientists make great endeavors to bring new materials, new devices, new tools and new methods to increase the knowledge on pathologies and to improve diagnosis and treatments. Concurrently, clinicians constantly request more precise information about their patients to take better therapeutic decisions. Both parties sometimes have difficulties in finding the time to share thoughts, hence a lack of communication often remains between clinicians and scientists. Moreover, the divergence of languages can be an obstacle. Tightening the links between the hospital and the laboratories through shared biomedical research projects could improve the medical care of patients, towards personalization at the individual level. This Ph.D. project fits within this context since it includes translational research based on real clinical needs. This work was indeed the fruit of a close collaboration between medical and engineering fields to ensure a beneficial contribution.

Two main research projects fed this thesis. The first was a three-fold project between three institutions: the University of Geneva/University Hospitals (UNIGE/HUG) led by Dr. Armand, the Ecole Polytechnique Fédérale de Lausanne (EPFL) led by Dr. Paraschiv-Ionescu, and the Centre Hospitalier Universitaire Vaudois (CHUV) led by Dr. Newman and was supported by the Leenaards Foundation (Lausanne, Switzerland) from 2015 until 2018. The overall goal was to design (EPFL's part), validate (UNIGE/HUG's part) and test in a clinical trial (CHUV's part) a wearable system for the physical activity and gait analysis of children with cerebral palsy. I was initially supposed to contribute to the UNIGE/HUG'part but as long as the project progressed, I finally had the chance to contribute to all of the three parts. Indeed, as an EPFL Ph.D. student, I undertook some system design -or more accurately system customization- projects belonging to the EPFL's part. And in 2018, as my fundings at UNIGE/HUG ended, Dr. Newman integrated me to his neuropediatric and neurorehabilitation research unit within the CHUV to take part in the clinical trial in collaboration with Dr. Gerber.
The second research project was a single and more autonomous project at UNIGE/HUG led by Dr. Armand and Dr. Fluss, neuropediatrician at the HUG, supported by La fondation Paralysie Cérébrale (Paris, France) from 2015 to 2017. Its goal was to evaluate the effect of cognitive-motor interferences in children with cerebral palsy.
At the end of these fundings, i.e. during the last year of my PhD, Prof. Aminian gave me the opportunity to contribute to a European project involving 34 research patterns supported by the IMI (innovative medicine initiative) foundation as he put me in charge of realizing a systematic review regarding the estimation of walking speed in real-life contexts. Besides, I was also involved in several other projects within the HUG, supported by the "Projets de Recherche et Development" program of the hospital, and the CHUV, supported by the Science for Smiles Foundation (Villeneuve, Switzerland), regarding physical activity and gait monitoring in free-living contexts for various populations.

Therefore, in this context, not only I collaborated with different institutions but I actually integrated several teams and took advantage of each of their expertise to make these projects bear fruit. Finally, this great opportunity of immersion in such high-level institutions, in tight collaboration with clinicians, allowed me to publish four peered-review articles during my thesis, submit one that is under review, and communicate in internal, national and European conferences several times, while building my Ph.D. project.

Abstract

Like 17 million people worldwide, an individual with cerebral palsy (CP) does not have the opportunity to walk harmoniously in society due to long-life impairments in movement and posture. The natural course of CP can be modulated by treatments and therapies that are nowadays mostly decided on the basis of assessments performed in clinical settings. The Clinical Gait Analysis (CGA) consists of a set of instrumented assessments aiming to obtain precise and quantitative information about a patient's gait deviations, in order to better identify his motor disorders and their possible causes. However, it is not clear whether gait assessments in clinics ('capacity') are representative of daily-life behaviors ('performance'). In this context, the present thesis aimed at exploring the gap between gait assessed in the laboratory and in real life for children with CP, as compared to children with typical development (TD). Two main objectives were settled: (i) to propose an objective and validated tool for gait assessments in a daily-life context with the highest possible accuracy as compared to clinical standard references; and (ii) to compare gait characteristics between both environments, the laboratory and the real life.

Considering the immense progress in the design of wearable sensors, notably inertial measurement units (IMU), great enthusiasm recently arose for their use in ambulatory monitoring. IMUs, including 3D accelerometers and gyroscopes, were thus exploited in this work as a solution to measure gait features in the children's daily life. A comparative study was first carried out to determine the most appropriate wearable system to be used for children with CP and for long-term measurements. Sensors located on the shanks and thighs and associated algorithms revealed to be the best solution. Next, a proof-of-concept study was completed and emphasized the need for personalized data processing for children with CP but also with TD. The second part (ii), dealing with the comparisons of walking capacity versus performance, adopted a progressive approach. The first step was the comparison between standardized walking, i.e. during a CGA protocol, and walking under challenging situations, such as dual tasks, i.e. thinking and talking while walking, in the laboratory. We found that dual tasks were responsible for lower motor gait capacities. The next step was the effective comparison of gait characteristics measured in the laboratory with the same gait characteristics measured in real-life settings, using the previously determined wearable system. First, walking speed, a global indicator of gait, and second, multiple gait parameters were compared between laboratory and daily life. Through two studies, we evidenced that children with CP have highly heterogenous behaviors but tend to perform better in clinical settings. Besides, we have highlighted that capacity is associated with performance in children with CP when they are evaluated with the same metrics.

Through this doctoral work, the great challenges of using IMUs for gait analysis of children with CP have been highlighted. The proposed solutions reached a compromise between accuracy, number of outcomes, and acceptance. Furthermore, the presented clinical results proved with objective and quantitative evidence the existence of a gap between gait assessed in the laboratory and gait in real life, which could help clinicians to devise therapeutic plans better tailored to each child's needs.

Keywords: walking, gait, cerebral palsy, clinical gait analysis, inertial measurement unit, dual task, capacity, performance, daily life, spatiotemporal parameters, speed, walking bout

Résumé

Tout comme 17 millions de personnes dans le monde, une personne atteinte de paralysie cérébrale (PC) n'a pas l'opportunité de marcher harmonieusement en société en raison de troubles du mouvement et de la posture. L'évolution naturelle de la PC peut être modulée par des traitements et des thérapies, qui sont à présent principalement décidés sur la base d'évaluations effectuées en milieu clinique. L'Analyse Quantifiée de la Marche (AQM) consiste en un ensemble d'évaluations instrumentées visant à obtenir des données précises et quantitatives sur les déviations de la marche du patient, afin de mieux identifier ses troubles moteurs et leurs causes possibles. Cependant, il n'est pas évident que les AQM (évaluant la 'capacité') soient représentatives des comportements du patient dans sa vie quotidienne ('performance'). Dans ce contexte, la présente thèse visait à explorer l'écart entre la marche des enfants atteints de PC évaluée en laboratoire et celle évaluée dans la vie quotidienne, par rapport aux enfants avec développement typique (DT). Deux objectifs principaux en ont découlés: (i) proposer un outil objectif d'évaluation de la marche avec la meilleure précision possible par rapport aux systèmes de références cliniques; et (ii) comparer la marche en laboratoire et en vie quotidienne sur la base de caractéristiques identiques.

Compte tenu des progrès dans le domaine des capteurs inertiels, leur utilisation dans l'évaluation de marche hors contexte clinique s'est récemment intensifiée. Les capteurs inertiels, formés d'accéléromètres et gyroscopes 3D, ont donc été exploités dans ce travail comme solution permettant de mesurer les caractéristiques de la marche dans la vie quotidienne des enfants. Une étude comparative a d'abord été menée pour déterminer le système de capteurs portables le plus approprié pour les enfants atteints de PC, pour des mesures de longue durée. Un système avec des capteurs situés sur les jambes et les cuisses a montré de bonnes performances. Ensuite, une étude « preuve de concept » a été réalisée et a souligné la nécessité de la personnalisation du traitement des données pour les enfants avec PC mais aussi avec DT. La deuxième partie (ii), consacrée aux comparaisons entre la capacité et la performance de marche, a adopté une démarche progressive. En premier lieu, nous avons comparé la marche standardisée, c'est-à-dire pendant le protocole d'AQM, avec la marche en situations difficiles, telles que lors de doubles tâches, à savoir penser et parler en marchant, en laboratoire. Nous avons constaté que les doubles tâches étaient responsables de diminutions de capacités motrices. Ensuite, nous avons comparé effectivement les caractéristiques de la marche mesurées en laboratoire avec celles mesurées dans des conditions réelles, à l'aide du système portable déterminé précédemment. Premièrement, la vitesse de marche, indicateur global de la qualité de marche, et deuxièmement, de multiples paramètres de marche ont été comparés entre le laboratoire et la vie quotidienne. A travers deux études, nous avons montré que les enfants atteints de PC avaient des comportements très hétérogènes mais semblaient avoir une meilleure qualité de marche en laboratoire. En outre, nous avons souligné que la capacité est associée à la performance chez les enfants avec PC quand elles sont évaluées par les mêmes métriques.

Durant cette thèse, les défis liés à l'utilisation des capteurs inertiels dans l'analyse de la marche des enfants atteints de PC ont été mis en évidence. Les solutions proposées ont abouti à des compromis entre précision, nombre de paramètres et acceptation. Par ailleurs, les résultats cliniques de cette thèse ont montré par des preuves objectives et quantitatives l'existence d'un écart entre les mesures en laboratoire et la vie réelle, ce qui pourrait aider les cliniciens à adopter des plans thérapeutiques plus adaptés aux enfants.

Mots clés: Marche, paralysie cérébrale, analyse quantifiée de la marche, capteurs inertiels, double tâche, capacité, performance, vie quotidienne, paramètres spatiotemporels, vitesse de marche, épisode de marche

Glossary

1-2-3D: one-bi-tri-dimensionnal
6MWT: 6-minute walk test
AFO: Ankle foot orthoses
AI: Asymmetry index
BCP: Bilateral cerebral palsy
BM: Biomechanical model
BoNT-A: Botulinim Neurotoxin-A
CDF: Cumulative distribution function
CGA: Clinical gait analysis
CI: Confidence interval
CMI: Cognitive motor interference
CNS: Central nervous system
COM: Center of mass
CP: Cerebral palsy
CPG: Central pattern generator
CV: Coefficient of variation
DL: Daily life
DT: Dual task
DTC: Dual task cost
EMG: Electromyography
ES: Effect size
F: Female
FFT: Fast Fourier transform
FS: Foot strike
FO: Foot off
FSR: Force-sensitive resistors
GC: Gait cycle
GCT: Gait cycle time
GDI: Gait deviation index
GGI: Gillette Gait Index
GMFCS: Gross Motor Classification System
GMFM: Gross Motor Function Measure
GNSS: Global navigation satellite system
GPS: Gait profile score
I: Integration
ICF: International classification of functioning, disability and health
IIR: Infinite impulse response
IMU: Inertial measurement unit
IQR: Interquartile range
LAB: Laboratory
M: Male
MAE: Mean absolute error
MEMS: Micro-electro-mechanical systems
MIMU: Magneto-inertial measurement units
ML: Machine learning
MRI: Magnetic resonance imaging
MS: Midswing
MVPA: Moderate to vigorous physical activity
PCA: Principal component analysis
PD: Parkinson's disease
PNS: Peripheral nervous system
Q1, Q3: first, third quartile
RMS: Root Mean Square
RMSE: Root Mean Square Error
ScT: simple cognitive task
SD: Standard deviation
SENIAM: Surface EMG for non-invasive assessment of muscles
Sh: Shanks (sensor configuration)
ShTh: Shanks and Thighs (sensor configuration)
SL: Stride length
SM: Statistical model
SmT: Simple motor task
STP: Spatiotemporal parameters
TD: Typically developing / Typical development
TO: Toe off
UCP: Unilateral cerebral palsy
VR: Virtual reality
WB: Walking bout
WHO: World Health Organisation
WS: Walking speed
ZUPT: Zero velocity update

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Part I

INTRODUCTION

This introduction part is composed of three chapters that set the context of the thesis. The first chapter introduces the clinical background from which the objectives of this thesis arise (end of Chapter 1). The second and third chapters set the state of the art regarding the two aspects of interest: gait measurement in the laboratory and gait measurement in the daily life.

Chapter 1

Introduction and outline of the thesis

Movements punctuate our lives. As emphasized by Etienne-Jules Marey in 1868, a french physiologist pioneer in motion analysis, movement is a constitutive function of living beings *(« Le mouvement est l'acte le plus important en ce que toutes les fonctions empruntent son concours pour s'accomplir »*[1] (Marey, 1868)). The understanding of human movement is thus a fascinating topic and remains fundamental for public health. We walk thousands of steps every day, perform dozens of posture transitions, and many other specific physical activities in professional or recreational contexts. Any alteration affecting movement is, therefore, a major issue for everyday life. There are innumerable causes of alterations; one of them, affecting 17 million people worldwide, is cerebral palsy (CP). Individuals with CP are characterized by heterogeneous lifelong motor disorders. Movement analysis helps to identify and understand their impairments. The most analyzed movement is gait as it is the most repeated movement day-to-day, and its analysis is facilitated by its cyclical aspect. However, gait assessed in standardized and supervised settings may not reflect real life.
This chapter describes the clinical context of the doctoral project and ends with the thesis objectives and outlines.

[1] «Movement is the most important act since it serves all functions for their accomplishment. »

1.1 Human locomotion

1.1.1 Generalities

Walking is the natural and most convenient mean of moving from one location to another along short distances (Perry and Burnfield, 2010), and is thus considered as a common and homogeneous ability among human beings.

Unlike most animal species, the human's gait maturates slowly (Ivanenko et al., 2007). A typically developing (TD) child acquires the ability to walk at the age of fifteen months on average and a mature gait pattern is established at the age of three years (Sutherland et al., 1980), and keeps maturing until the age of eleven (Gouelle, 2012). This slow maturation is believed to be associated with the complex development of the central nervous system (CNS) and the challenge of bipedal walking (Ivanenko et al., 2007).

Bipedal gait is a succession of body segments movements leading to the propulsion and the forward progression of the body while keeping balance (Perry and Burnfield, 2010) which is permitted by the presence of terrestrial gravity. The gravitational force induces a pendulum-like behavior while walking (Cavagna et al., 1976; Courtine et al., 2006). Gait is thus a cyclical activity and for each cycle, series of interactions between two, right and left, multi-segmented lower limbs and the total body mass occur (Perry and Burnfield, 2010).

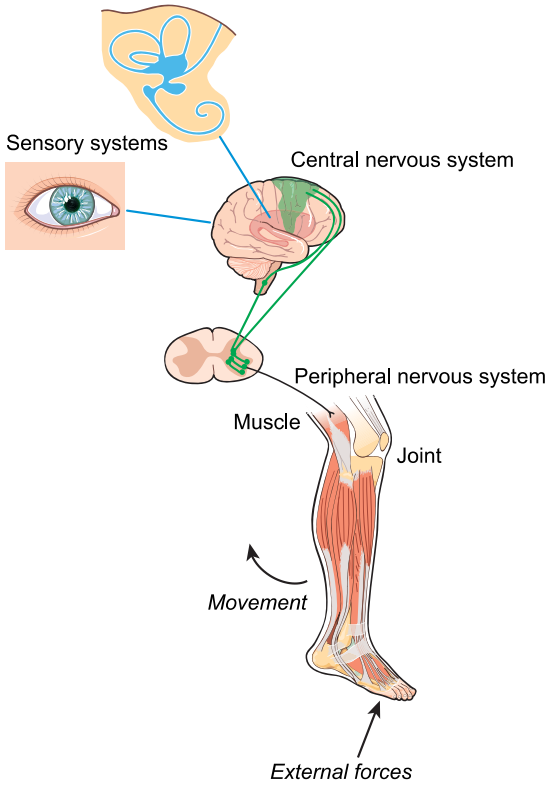
Natural walking is influenced by many factors such as cultural norms, natural constraints, individual personality, emotions, and fashion phenomena, resulting in innumerable ways of walking (Troje, 2002).

1.1.2 Criteria for quality of life

The ability to walk guarantees functional independence, and therefore social integration (Hausdorff and Alexander, 2005). 'Participation' as described by the World Health Organization (WHO) is the "involvement in a life situation" (World Health Organization, 2002). The ability to walk safely, efficiently, harmoniously and aesthetically is highly related to participation, thus to quality of life and well being (Cuomo et al., 2007). Walking speed has been considered as the 6th vital sign as it is a reliable, valid, sensitive and specific measure to predict health status and functional decline (Orendurff et al., 2008). Walking speed is associated with quality of life (Orendurff et al., 2008).

1.1.3 Physiology

Gait is a complex phenomenon involving various organ systems. Any movement is indeed operated through a hierarchical chain of commands from the motor cortex to the muscles. The sensory systems (visual, auditory, vestibular, somatosensory, etc.) send information, through many excitatory and inhibitory neural junctions to the CNS, which is processed by the cerebral areas and relayed to the spinal cord. Individual motor units bring the information from the spinal cord to the skeletal muscles so that they activate to generate action at the joint level, thus creating movement (Figure 1). The spinal cord is also the setting of motor reflexes (Gage et al., 2009). Rhythm and pattern of locomotion are controlled by a spinal interneuronal network, called "central pattern generators" (CPG) (Takakusaki, 2013). Considering the numerous systems involved in the movement generation, a precise understanding of the causes of an altered movement can be challenging (Armand et al., 2014).



Adapted from (Armand et al., 2014)

Figure 1 - Organ systems involved in movement generation

1.1.4 Pathological locomotion

Since gait is the result of coordination between various organ systems, a great variety of issues altering one or several of these systems can result in gait disorders: from a thorn piercing the skin to the result of a stroke. The following are the most common alterations or pathologies affecting gait function.

1.1.4.1 Aging

Mobility limitations are very frequent among older adults and are inevitable during aging. From around 10% of adults between the ages of 60 and 69 to more than 60% in adults over 80 years experience gait and balance disorders (Pirker and Katzenschlager, 2017). The various causes of gait disorders associated with age are impaired proprioceptive functions, impaired vision, vascular encephalopathy and joint osteoarthritis (Pirker and Katzenschlager, 2017) inducing decreased muscle force and lack of attention. Elderly people thus need to adopt protective strategies while walking (widening and shortening the steps, prolonging the contact with the floor, lifting lower the feet, slowing down, etc.) to avoid falls. Indeed, 30% of community-dwelling persons over 65 years old experience at least one fall per year (Tinetti et al., 1988). Falls are a major cause of functional decline and mortality among the elderly population (Tinetti et al., 1990), so they constitute a major public health concern nowadays with ageing populations.

1.1.4.2 Neurological disorders

The most known neurological disorders associated with gait disability are Parkinson's disease (PD), multiple sclerosis, cerebral palsy (CP) and stroke. PD is a neurodegenerative, progressive and chronic disease of the basal ganglia inducing limbs tremor, rigidity stiffness, bradykinesia (slow movements) and postural instability (Fatmehsari and Bahrami, 2010), inducing difficulties in gait initiations, slow and highly variable gait with short steps, a narrow base of support and a stooped posture (Pirker and Katzenschlager, 2017; Plotnik et al., 2007). Patients with PD experience "freezing of gait" episodes when meeting obstacles or narrow paths (Pirker

and Katzenschlager, 2017). PD has a prevalence of between 100 and 300/100,000 (Elbaz et al., 2016). Multiple sclerosis is an immune-mediated disease characterized by inflammatory demyelination and axonal damage of the CNS. Neuronal pathways are delayed or blocked, inducing gait impairments notably with altered spatiotemporal (pace) parameters (Moon et al., 2017). Multiple sclerosis induces ataxic gait characterized by irregular and poorly coordinated lower limbs movements, variable step length, and slight stoop (Pirker and Katzenschlager, 2017). The global median prevalence of multiple sclerosis reached 33/100,000 in 2013 (Leray et al., 2016). Strokes result from an excessive (hemorrhagic stroke, 20% of the cases) or insufficient (ischemic stroke, 80% of the cases) amount of blood within the cranial cavity, providing inadequate oxygenation to the brain. Stroke survivors experience diverse sensorimotor impairments such as muscle weakness, impaired selective motor control, spasticity, and proprioceptive deficits that hinder normal gait (Balaban and Tok, 2014). Fifteen million people suffer from stroke every year (Yang et al., 2013). CP is caused by early damage to the developing brain (before, during or just after birth). With a prevalence of 1.8/1,000 live births, CP affects 17 million people worldwide (Graham et al., 2016). The major consequences of the brain injury in CP are motor control dysfunction, abnormal muscle tone, paresis and joint contractures (Perry and Burnfield, 2010). These impairments induce various altered gait patterns which are detailed in the following sections.

1.1.4.3 Muscle disease

Congenital or acquired myopathy induces muscular dystrophy and muscle weakness. Patients suffering from myopathy generally present waddling gait characterized by excessive lateral trunk movements and lower limbs circumduction to compensate for pelvic girdle and gluteal weakness, also called ‘Trendelenburg’ gait (Chen et al., 2016). They can also compensate a drop foot by excessively flexing the knee to make a step. Gait speed and step length are thus highly reduced. The most frequent myopathy in adults is myotonic dystrophy affecting 0.5–18.1/100,000 cases, and in children is Duchenne muscular dystrophy affecting 1.7–4.2/100,000 newborns (Theadom et al., 2014).

1.1.4.4 Osteoarthritis

Osteoarthritis is a joint disease caused by damage to the cartilage and underlying bone (due to biomechanical and/or biochemical factors). The major manifestation is pain (National Collaborating Centre for Chronic Conditions, 2008) inducing reduced gait speed, reduced range of motion of the damaged joint, and a decreased loading on the affected limb (Tadano et al., 2016). Osteoarthritis leads to an asymmetric (limping) gait. In severe osteoarthritis, total joint arthroplasty (joint replacement) can be advised, to reduce pain and restore gait function. Hip and knee arthroplasty are the most frequent total joint arthroplasty. Osteoarthritis is the most common form of arthritis. The global incidence of knee and hip osteoarthritis was estimated in 2016 by the Global Burden of Disease study at 199/100,000 cases (vizhub.healthdata.org).

1.1.4.5 Orthopedic corrective treatments

Orthopedic corrective treatments such as amputation and arthrodesis also induce gait abnormalities. The major causes of amputations are traumatic and diabetes-related vascular amputations (78-704/100,000 amputees in the diabetic population (Narres et al., 2017)) (Kark et al., 2012). Gait symmetry is highly impacted in case of lower limb amputation (Kark et al., 2012).

This is a non-exhaustive list of causes of pathological gait. CP is one of the most studied pathologies in research (Figure 2), but is also one of the populations with the highest hope regarding expected effects of surgical treatments and rehabilitation programs, since it affects patients from an early age. This is why this thesis was dedicated to the study of gait in CP.

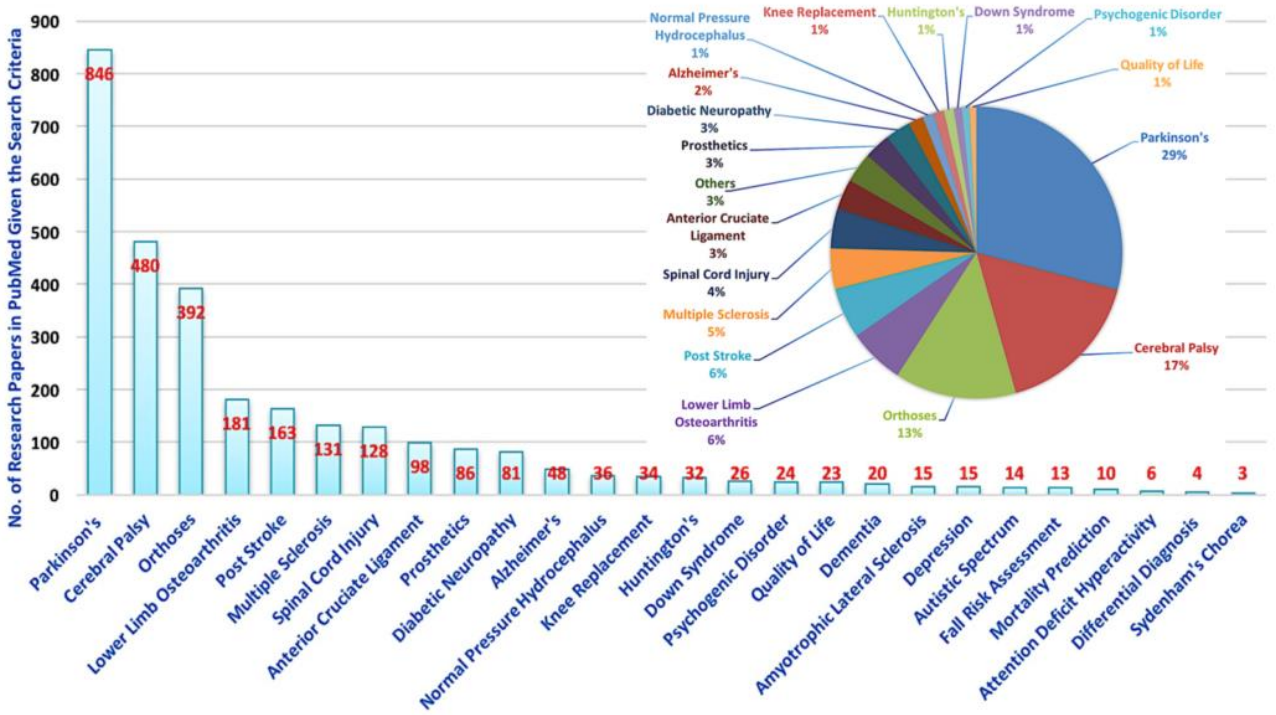


Figure 2 - Distribution of research efforts regarding gait pathologies between 1970 and 2016 (Chen et al., 2016)

1.2 Cerebral palsy

The term ‘cerebral palsy’ refers to a clinical condition with shared developmental features rather than a disease entity (Graham et al., 2016). CP comes from irreversible brain injury during its development (pre, peri or neonatal) leading to a loss of motor control and abnormal musculoskeletal development. CP is the most frequent physical disability in childhood, affecting 1.5-2/1000 live births in European countries (Johnson, 2002) and with an equivalent prevalence of 17 million people worldwide (Graham et al., 2016).
CP causes movement difficulties which can considerably limit daily activities throughout life. Because of their altered motor function, certain children with CP can hardly walk. In fact, only two-thirds of these children are able to ambulate in society with or without mechanical aids (Beckung et al., 2008).

1.2.1 Definition

CP was first described by J.-B. Cazauvieilh (French psychiatrist) in 1827 (at the time called "congenital paralysis") (Chabrier et al., 2019). Thereafter, the definition and the appellation have evolved a lot and still remain debated (Chabrier et al., 2019). The latest and most accepted definition was delineated by an international group led by P. Rosenbaum and M. Bax in 2005 and stated: “*CP describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication and behaviour, by epilepsy and by secondary musculoskeletal problems*” (Bax et al., 2005).

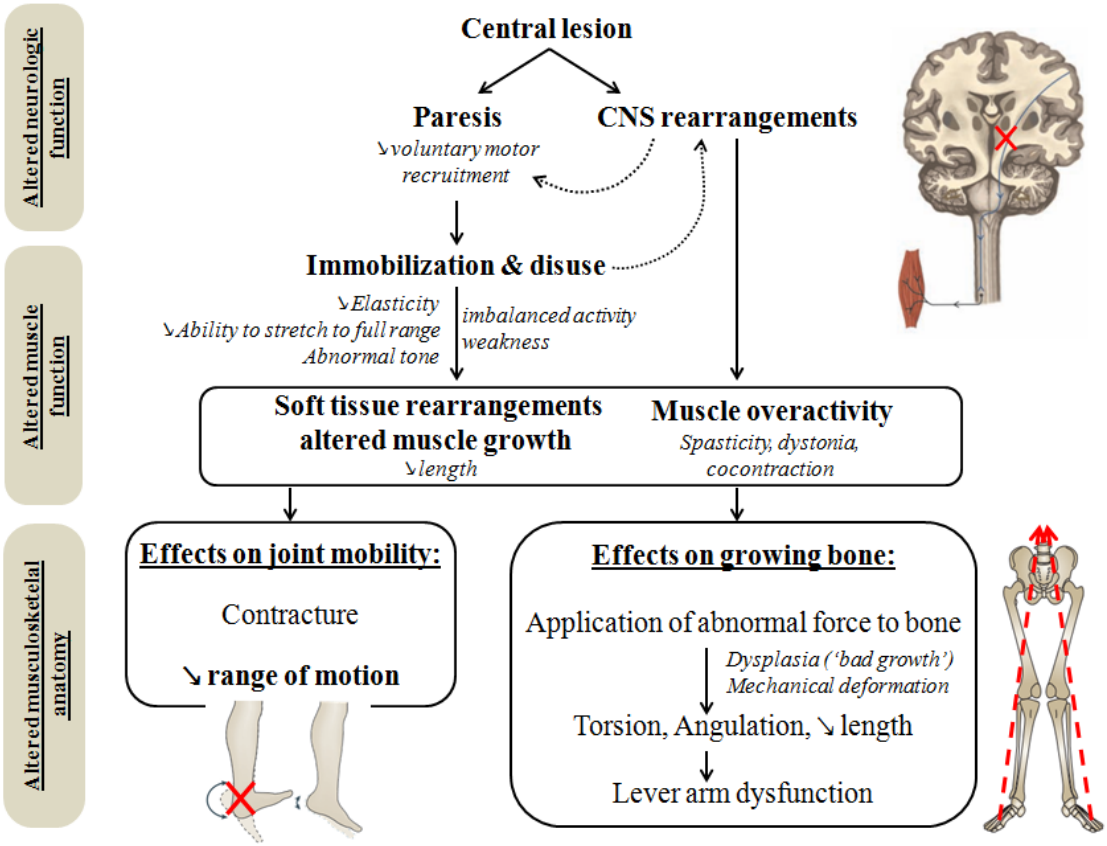
1.2.2 Etiology

There is no precise and fixed etiology for CP. Indeed, encephalic lesions causing disability can be localized in different areas, occur at different stages of brain development and be more or less severe. It is worth mentioning that the cause of CP remains unknown in certain cases. Hypoxia, infection, stroke or hypotension are the most

frequent causes of brain injury encountered in CP (Wimalasundera and Stevenson, 2016). Injuries happening in-utero (e.g. infection, genetic mutation, white matter disease, hypoxia, hypotension, hemorrhage, asphyxia and stroke) account for 80% of CP, hypoxia during delivery accounts for 10% of CP, and post-neonatal injuries (e.g. infection, hypoglycemia, stroke, accidental or non-accidental trauma) account for 10% of CP (Wimalasundera and Stevenson, 2016).
Premature birth and difficult delivery are the two main risk factors of CP (Graham et al., 2016). Pre-term birth before 28 weeks of gestation increases the risk of CP by 50 as compared to full term birth (Graham et al., 2016).

1.2.3 Motor disorders

CP covers a wide range of clinical presentations depending on the timing and the severity of the brain injury. Practically, no child with CP is identical to another. However, the general causal links resulting from alterations of brain function lead to, as depicted in Figure 3, changes in muscular activity and motor function, which influence the development of the skeleton.



Scheme adapted from (Gage et al., 2009; Gracies, 2005a, 2005b), pictures taken from (Gage et al., 2009; Graham et al., 2016)

Figure 3 – Scheme of causal links resulting from an altered neurological function

As illustrated in Figure 3, an impaired neurological function alters musculoskeletal anatomy through muscle function alterations. The central (brain) lesion induces paresis, i.e. decreased voluntary skeletal motor unit recruitment (Gracies, 2005a). This imposes the immobilization of the paretic limb in a shortened position, leading to adaptive structural changes of the muscle fibers and eventually shortening of the muscles. The induced disuse of the limb causes delayed plastic rearrangements in the CNS and the muscle itself, exacerbating the baseline paresis (Gracies, 2005a). Muscle alterations are mostly stiffness, abnormal length and tone. This causes joint immobility (contracture) and abnormal forces applied to the bones which eventually

alter the musculoskeletal anatomy (length, torsion, displacement and dislocation). The most known form of muscle tone increase is spasticity. This is one of the major problems in patients with a damaged CNS. Spasticity is defined as a speed-dependent increase of the myotatic reflex in response to passive movement (Biering-Sørensen et al., 2006; Gracies et al., 2010). This is due to a lack of inhibition of the spinal reflexes, induced by damage to the motor cortex and/or cortico-spinal tract.

Pathological gait resulting from these altered functions is a mix between primary, secondary and tertiary abnormalities (Berker and Yalçin, 2008; Gage et al., 2009) (Table 1), which must be well discriminated for a good understanding of the problems arising in CP (Aisen et al., 2011). The primary abnormalities are directly related to the brain damage and are not curable. The secondary abnormalities develop with time in response to the primary impairments and can be corrected. The tertiary abnormalities are the results of strategies to adapt to the secondary impairments (Berker and Yalçin, 2008). The tertiary abnormalities should not be corrected since they disappear once the secondary abnormalities are fixed.

Table 1 - Primary, secondary and tertiary abnormalities in CP

Primary abnormality *(permanent)*	**Secondary abnormality** *(can be corrected)*	**Tertiary abnormality** *(disappear spontaneously if secondary abnormality corrected)*
- Paresis - Loss of selective motor control - Impaired balance - Abnormal tone	- Muscle contracture - Abnormal bone growth - Muscle weakness	- Compensations - Pain

1.2.4 Associated disorders

Children with CP can exhibit not only a range of motor disorders but also associated impairments including cognitive disorders (50%), epilepsy (25%), speech disorders (25%), incontinence (25%), sleep disorders (20%), behavior disorders (20%) and visual disorders (10%), among others (Mandaleson et al., 2015; Novak, 2014).
Life expectancy approaches that of general population (Aisen et al., 2011) but depends on the number and the severity of these associated impairments (Wimalasundera and Stevenson, 2016).

1.2.5 Classifications

It can prove challenging to classify individuals with CP, since they have various etiologies and manifestations. Three main approaches exist which are described is this section.

1.2.5.1 Topography of the motor disorders

Sub-types of CP regarding the topography of the motor disorders are monoplegia, hemiplegia, diplegia, triplegia and quadriplegia (Figure 4). Monoplegia (rare) corresponds to one affected lower limb. Hemiplegia is characterised by the alteration of 2 limbs of the same side of the body (lower and upper limb) whereas diplegia is characterized by the alteration of 2 limbs of both sides (both lower limbs). Triplegia and quadriplegia corresponds to 3 and 4 affected limbs respectively. This classification has its limitations because it is possible to find functional deficiencies on the non-hemiplegic side or non-impaired limb. A twofold classification distinguishing patients with unilateral and bilateral CP (UCP and BCP) is more commonly used

nowadays. Indeed, UCP results from unilateral brain infarct mainly caused by traumatic, vascular, or infectious lesion, whereas BCP comes more often from severe perinatal asphyxia or from periventricular leucomalacia (necrosis of white matter), commonly in low-birth-weight babies (Berker and Yalçin, 2008).

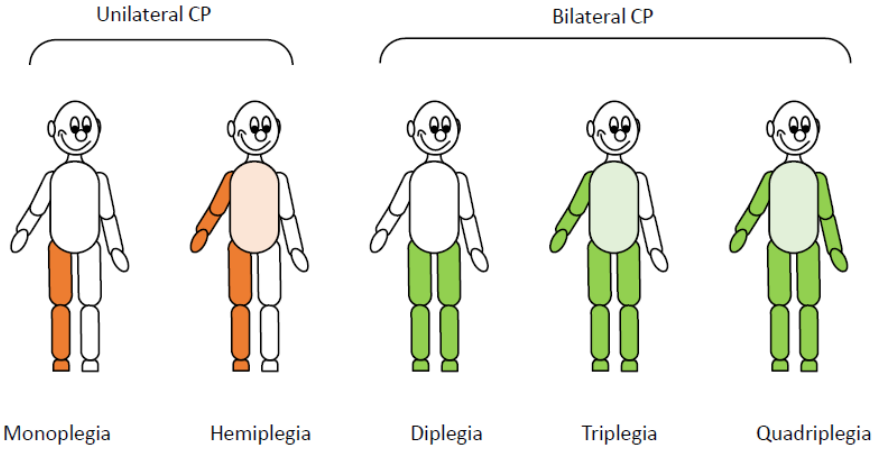
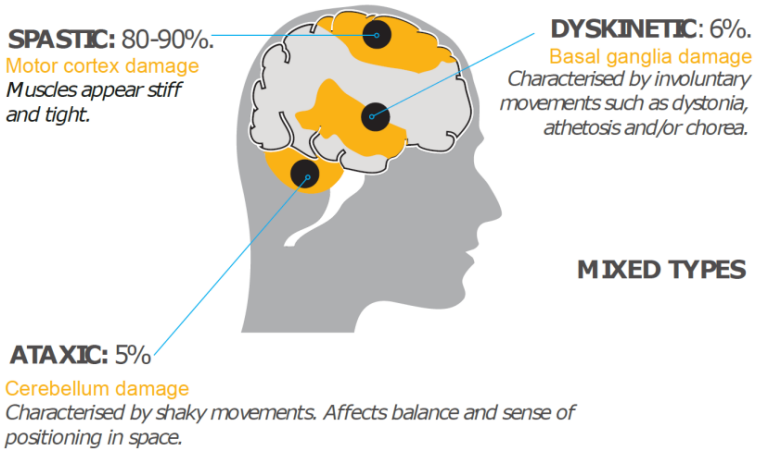


Figure 4 - Topographical description of cerebral palsy

1.2.5.2 Typology of motor disorders

According to the localization and the type of the brain lesion, different types of motor disorders can predominate in CP. The three major groups are the spastic, dyskinetic and ataxic forms of CP, and a fourth group which describes a mixed form of the previous ones (Graham et al., 2016) (Figure 5). The spastic form of CP, the most common, arises from damage of the motor cortex, as described in section 1.2.3. About 80-90% of CP children have spasticity (O'Shea, 2008). The dyskinetic form, which accounts for 5-10% of the cases, arises from damage to the basal ganglia, and is characterized by muscle stiffness and involuntary movements (O'Shea, 2008). Finally, the ataxic form, which represents 5% of the cases, arises from cerebellum damage and is characterized by non-accurate shaky movements (O'Shea, 2008).



Adapted from a World Cerebral Palsy Day infographics (worldcpday.org)

Figure 5 - Typology of motor disorders according to the localisation of the brain damage

1.2.5.3 Gross motor function

In the past, the level of motor function impairments in CP was classified using expressions like "independent", "crutch-aided", "walker-aided", or "wheelchair-aided" (Schwartz and Munger, 2018) before being widely substituted with the Gross Motor Classification System (GMFCS) introduced in 1997 (Palisano et al., 1997).

It consists of a 5-level classification describing the gross motor function of the child with regard to his age, based on his self-initiated movement capacities (Mandaleson et al., 2015). The description of the GMFCS levels depends on age but can be generalized as follows (Figure 6):

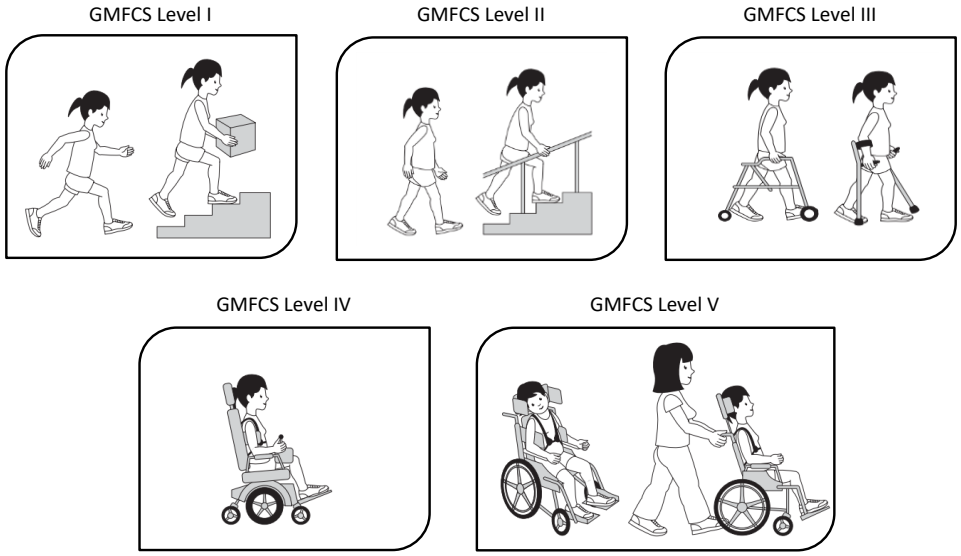
GMFCS level I: Children can walk, run, jump, climb stairs, and carry objects in all settings without limitation, but are limited in complex motor activities.

GMFCS level II: Children can walk in most indoor settings but with difficulties. They are limited in outdoor settings, for long distances.

GMFCS level III: Children can walk using a mobility device in most indoor settings and uses wheeled mobility for long distances.

GMFCS level IV: Children can move thanks to a physical assistance or power mobility in most settings.

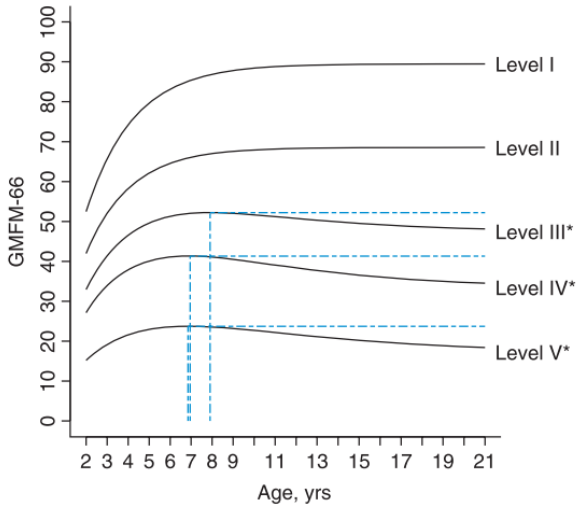
GMFCS level V: Children can move only if they are transported in a wheelchair with head and trunk support by a tertiary person.



Adapted from (Reid et al., 2015)

Figure 6 - Gross Motor Function Classification System (GMFCS) levels

This classification system is the most used classification but it suffers from several drawbacks; one of them being its impermanence since motor function evolves in time (Schwartz and Munger, 2018). For instance, Schwartz and Munger (2018) reported that among 562 patients assessed, 23% changed GMFCS levels at least once due to natural evolution or after a treatment. Indeed, the GMFCS level can change with increasing age. Young children have a faster progression in gross motor function than older children as illustrated on Figure 7, which represents the evolution of the gross motor function (evaluated by the GMFM, a clinical score that is introduced in section 1.3.1) with regard to age and GMFCS level. Children with lower levels of GMFCS (e.g. I and II) have a longer evolution of gross motor function than those with higher levels whom maximal levels of motor function are reached earlier. Although widely used in clinical practice, research, teaching and administration (Palisano et al., 1997), this classification is quite confusing since boundaries between two levels are very thin and also, the inter-rater reliability is only fair to good (Palisano et al., 1997). Also, from one day to another, a child's gross motor function can slightly vary and clinicians may interpret the classification descriptions differently.



**GMFCS levels with significant decline with age, and dashed lines illustrate age at maximum gross motor function level*

Figure 7 - Gross Motor Function scores evolution according to age and Gross Motor Function Classification (GMFCS) level (Hanna et al., 2009)

1.2.5.4 Gait patterns

As previously mentioned, patients with CP present multiple various gait patterns. However, similarities can be observed among unilateral spastic and bilateral spastic CP. Various classifications based on the kinematics of the lower limbs (mainly in the sagittal plane) have been proposed. A recent systematic review (Papageorgiou et al., 2019) has identified six consensual multiple joint patterns which were originally introduced by Rodda et al. (Rodda and Graham, 2001; Rodda et al., 2004), Winters et al. (Winters et al., 1987) and Simon et al. (Simon et al., 1978). These patterns are depicted in Figure 8. They consist in a progression in the severity and the localisation (from distal to proximal) of the impairments (Armand et al., 2016).

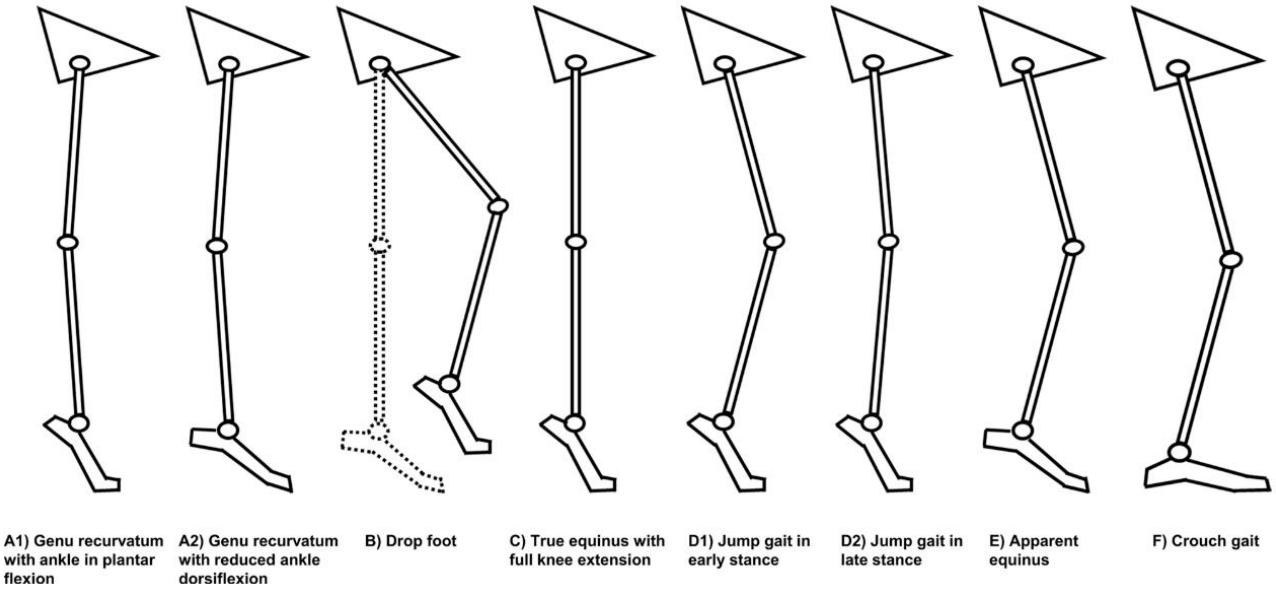


Figure 8 - Gait patterns classification in cerebral palsy (Papageorgiou et al., 2019)

Type A is characterized by a full knee extension or hyper-extension (recurvatum) during stance with impaired ankle motor control resulting in permanent plantar flexion (equinus) in type A1, or reduced dorsiflexion in

type A2. Type B is characterized by a drop foot during the swing phase. Type C is characterized by an equinus during stance. Type D, called 'jump knee', is characterized by an equinus and excessive hip and knee flexions in early stance, followed by hip and knee extension to a variable degree in early stance for type D1, or late stance for type D2. Type E is characterized by excessive flexion of the hip and the knee with a normal range of motion of the ankle. Finally, Type F, called 'crouch gait', is characterized by excessive flexion at ankle (dorsiflexion), knee and hip levels as well as excessive pelvic anteversion or retroversion.
Importantly, for bilateral spastic CP, different groups can be attributed to each limb of the same patient (Rodda and Graham, 2001).

1.2.6 Management of CP

CP is not curable but the consequences at the musculoskeletal level can be managed. Usually, children with CP follow treatments throughout their childhood. The main treatment options are physiotherapy, pharmacology, orthotics and surgery. Physiotherapy is recommended to the children as soon as they are diagnosed with CP (Graham et al., 2016), and is the most common treatment in CP (Armand et al., 2016). Physiotherapy aims at training the upper and/or lower limbs to maintain or restore adequate ranges of motion, to improve muscle strength, balance and coordination (Armand et al., 2016) in order to guarantee the best functional abilities and maximize participation in daily life. Spasticity management is commonly addressed by injections of Botulinim Neurotoxin-A (BoNT-A) inside the muscle (Fairhurst, 2012). The benefit for the children is short-term. BoNT-A injection benefits in the long term are not well understood (Graham et al., 2016). Spasticity is also commonly managed by Baclofen medication, administered orally or intrathecally (into the spinal canal) (Papavasiliou, 2009). Orthoses and other rehabilitative technologies such as robotic devices, aim at facilitating ambulation, by providing the necessary support. For example, ankle foot orthoses (AFO) are very common in children with CP to restore normal ankle rockers, thus improve their gait efficiency (Graham et al., 2016). Orthopedic surgery is often advised to correct contractures, bone deformities or joint displacement (Nicholson et al., 2018). For examples, muscle-tendon unit lengthening helps increasing joint range of motion and rotational osteotomy fixes the bone in an appropriate position and restores lever arm. Current best practices are to perform single event multilevel surgery to fix multiple abnormalities during a single surgical procedures, avoiding piecemeal annual surgeries (Fairhurst, 2012), often called the 'birthday syndrome' (Armand et al., 2016; Chang et al., 2010; Švehlík et al., 2016). Finally, selective dorsal rhizotomy is a surgical procedure to manage spasticity. It consists of a resection of nerve rootlets of the dorsal column, reducing afferent and efferent activity of the reflex arc (Berker and Yalçin, 2008), providing a permanent and global reduction of the lower limbs' muscle tone (Armand et al., 2016). It is worth mentioning that most children have to undergo several procedures (surgery, injections, etc.) throughout childhood since the musculoskeletal alterations keep progressing.

Generally, spasticity reduction through BoNT-A injections is advised between 5 and 8 years of age (Gage et al., 2009) and surgical interventions are advised at later stage, after the peak of the pubertal growth spurt, around 10 to 12 years of age (Švehlík et al., 2016). In addition, a recent interest was taken in early interventions, i.e. during the first postnatal years, for infants diagnosed with CP. They consist in light interventions such as parent education, environment modification, social scaffolding, inhibition of abnormal motor patterns, facilitation of normal motor patterns, etc. (Morgan et al., 2016). Although variable results were reported in the literature, early interventions in CP showed overall moderate to large effects on motor outcomes (Hadders-Algra et al., 2017; Morgan et al., 2016).

Traditional management of motor disabilities aimed at providing a motor pattern as 'normal' as possible, and it has been shown that it was not always aligned with the family and the child's wishes and expectations (Thomason et al., 2018). Current practices are now moving toward a management of the disability taking into account the child's aspirations. For this purpose, the Gait Outcomes Assessment List (GOAL) was recently (2014) developed by a multidisciplinary team in Canada to assess gait priorities and functional mobility of ambulant children with CP (Thomason et al., 2018). This may lead to new intervention programs with a more appropriate family-centered approach.

1.2.7 CP and participation

CP is the most frequent cause for physical disability in childhood, meaning that activity limitation is a key element to consider (Cans et al., 2008; Rosenbaum et al., 2006). Children with CP have restricted participation ("involvement in a life situation" (World Health Organization, 2002)) in daily activities and social interactions which are associated with the severity of the motor and neurological impairments (Beckung and Hagberg, 2002; Fauconnier et al., 2009). Four factors have been identified as contributing to participation among children with disabilities: having fun, being successful, doing things on their own and being with others (Omura et al., 2018).

During adolescence, children with CP, just like TD children, overcome great physical and psychological changes associated with puberty [12]. Due to their disability, these changes are often slower for children with CP, leading to greater psychological challenges (Dang, 2012). Participation, as well as well-being, of adolescents with CP can rapidly be impacted. Maintaining a good level of participation is thus of major importance for therapists taking care of children with CP.

1.2.8 Summary of CP characteristics

The most important characteristics defining CP are reported in the following table.

Table 2 - Summary of characteristics of CP

CP is …

A description of clinical conditions rather than an etiological diagnosis (umbrella term: large number of causes, and large range of severity)	Mainly manifested with motor disorders but can be accompanied by many disorders such as cognitive, behavioural, visual, epileptic or language impairments
The neurological consequence of lesions or bad development of the central nervous system during early life	Not curable but the manifestations can be treated progressively through surgery, orthotics, medication and/or physiotherapy
The consequence of a non-progressive and definitive injury	The cause of decreased levels of physical activity and participation
The most frequent motor disability in children	Traditionally categorized into 5 groups of gross motor function (GMFCS levels)
Characterized by variable manifestations over time	A lifelong disability
Leading to an inability to walk in 1/3 of cases	

(Icons from flaticon.com)

1.3 Gait evaluation

1.3.1 Scale-based evaluations

Gait deviations can be assessed by diverse tools which have different levels of accuracy. Scale-based evaluations and questionnaires exist to provide a global description of functional mobility. Among the existing questionnaires assessing gait function (functional mobility), among other functions, the most used are the Gillette Functional Assessment Questionnaire (FAQ) which assesses the child's level of functional mobility on 32 items (Schiariti et al., 2014a), the Pediatric Evaluation of Disability Inventory (PEDI) which assesses the child's functional capabilities by observing his mobility, self-care and social function (Schiariti et al., 2014a) and the Functional Mobility Scale (FMS) which scores functional mobility over three distances (5, 50 and 500m) (Graham et al., 2004). Two known scales are dedicated to the observation of the gait pattern: the Physician Rating Scale (PRS) and the Edinburgh Visual Gait Analysis Interval Testing (GAIT) (Maathuis et al., 2005). These two scales were developed to quantify walking pattern of children with CP using a simple and standardized tool based on video recordings (Maathuis et al., 2005). Indeed, video based observations are suitable to perceive the most important deviations in a simple and non-expensive way. PRS and GAIT scales were found to have excellent intra-observer reliability, however, poor inter-observer reliability (Maathuis et al., 2005). Indeed, a component of subjectivity inherently introduces some bias to these assessments.
The Gross Motor Function Measure (GMFM) is a standardized observational instrument to measure change in gross motor function over time (Smits et al., 2014; Van Eck et al., 2009). It consists of 88 or 66 items, depending on the version, assessing five activity domains which are lying and rolling, sitting, crawling and kneeling, standing, walking, running and jumping. GMFM is one of the few validated tools, with high inter observer and test-retest reliability, to measure responsiveness of a treatment (Alotaibi et al., 2014; Ko, 2014). It is considered as the gold standard for assessing function (Schwartz and Munger, 2018), hence highly used in clinic and research.

1.3.2 Clinical gait analysis

In addition to the previous global gait evaluations, patients with walking disorders are commonly invited to perform an instrumental evaluation of their gait function called Clinical Gait Analysis (CGA). CGA is a clinical examination aiming to obtain precise and quantitative information about the motor capacities of a patient, in order to better identify and understand his motor disorders and the possible causes (Moissenet and Armand, 2015). The analysis is composed of a wide range of instrumented measurements of gait features, as well as a physical examination to evaluate passive range of motion, muscular spasticity, selectivity and strength. The instrumented gait analysis mainly includes the recording of kinematics, kinetics, muscular activation and plantar pressures during walking. The patient walks barefoot along a walkway at his self-selected speed while being recorded. CGA is carried out in a dedicated laboratory since it requires specific and advanced equipment. Chapter 2 is dedicated to technical and practical details about CGA.

1.3.2.1 Drawbacks in view of WHO's considerations

The WHO, in its classification of health and health-related domains: the International Classification of Functioning, Disability and Health (ICF), considers three domains for a health condition definition: body structure and function, activities and participation (Figure 9) (World Health Organization, 2002). These domains are modulated by environmental and personal factors. In this context, the ICF defined two qualifiers for describing activities and participation: 'capacity' and 'performance'. Capacity describes *what a person can do in a standardized situation* and performance describes *what a person actually does in his actual*

environment (World Health Organization, 2002). The WHO suggests that regardless of the pathology, both domains have to be evaluated.

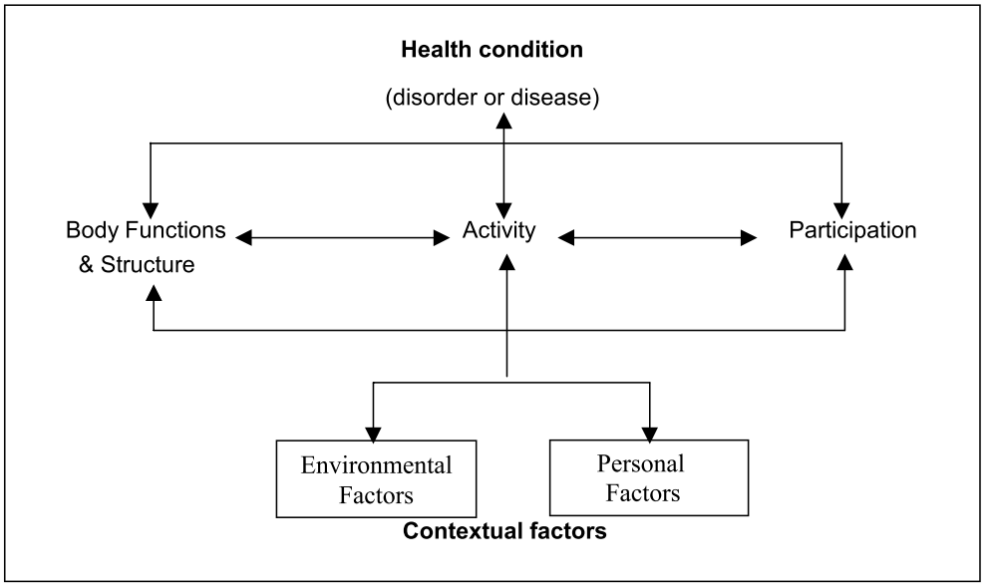


Figure 9 – The ICF's model of health condition (World Health Organization, 2002)

CGA can be considered as a tool to connect the '*body, functions and structures*' to the walking '*activity'*. Even if CGA is nowadays the most accurate and complete way to evaluate gait deviations, such an assessment is not likely to be a real representation of the patient's usual mobility, his 'performance'. Although an infinite number of interpretations of 'capacity' can arise from the above-mentioned WHO's definition, walking during CGA must describe gait capacity, since it reflects the level of functioning in a standardized environment.

Through CGA, therapeutic decisions are made on the assumption that capacity is equal to performance whereas they must diverge (Smits et al., 2014). First, the clinical measurements can only be carried out during a short period of time and at a particular moment of the day. Second, the laboratory has a predefined specific path where the patient walks only a few steps surrounded by numerous cameras. Therefore, in such a situation, the patient's level of functioning can either be improved, if he shows the best of himself, or be hindered because of discomfort and stress. It has been demonstrated that this behavior can be part of a known phenomenon called the 'Hawthorne effect', being the tendency to substantially change the manner in which symptoms are expressed while simply being observed by a caregiver or a health worker (Berthelot et al., 2011). Several studies have highlighted the difference between capacity and performance by exploiting the relationship between the scores of questionnaires such as those mentioned in the previous section (FMS, PEDI, FAQ, GMFM, etc). It has been demonstrated that patients with equivalent levels of capacity can have different levels of performance (Holsbeeke et al., 2009): capacity is shown to exceed performance (Young et al., 1996). Environmental factors, including physical (home and school settings for instance), social (family, teacher support) and personal (motivation, choices, personality) factors, are likely to be responsible for this distinction (Gosselin et al., 2018; Smits et al., 2014).

1.3.3 Alternatives to clinical gait analysis

To overcome the lack of representativeness of the gait assessment during standard CGA, several alternatives are currently emerging.

1.3.3.1 Challenging gait

As compared to straight and spontaneous gait, many activities such as walking at different speeds, on uneven surfaces or on inclined planes have the advantage to recruit different musculoskeletal functions, to reach closer to the joint range of motion limits and, above all, to be more representative of a daily-living situation. These kind of 'daily-life like' activities, reproducible in clinical settings, are relevant to give a better insight of the patients' usual mobility (Komnik et al., 2015). The following table reports various examples of protocols assessing gait in challenging situations (Table 3).

Table 3 - Examples of challenging gait protocols doable in laboratory settings

Protocol	Description	Expected challenged gait features	Study examples
Stairs	Climbing and descending stair steps	Increased ranges of motion and higher muscular activity leading to higher forces and moment in the joints	(Bar-Haim et al., 2019)
Tandem gait	'Heel-to-toe' walking on a line	Reduced base of support causing instability	(Bisi et al., 2019; Speers et al., 1998)
Fast gait (e.g. 6 minute walk test (6MWT))	Walking as fast as possible	High intensity of activity related to physical endurance	(O'neil et al., 2013)
Turning gait	Turning while walking	Lower stability and gait control	(Dixon et al., 2016)
Dual task*****	Performing a concurrent motor or cognitive task while walking	Cognitive-motor or motor-motor interferences resulting in decreased gait performance	(Katz-Leurer et al., 2014)

******* *detailed in the following section*

With the idea of evaluating challenging gait, protocols based on virtual reality interfaces have been developed recently. This technological tool has especially been used for rehabilitation, promoting motivation to the young patients (Aisen et al., 2011). But it also has the potential to be used for simulating daily life activities in the context of in-laboratory gait analysis. A study of van der Krogt et al. (2014) have notably observed, based on parent's remarks, that the gait of children with CP on a treadmill under VR environment better resembled to their gait in daily life. Deeper investigation in this area should be undertaken, especially because it is well established that walking on a treadmill is not reflective of walking overground (Degache et al., 2014; Van Der Krogt et al., 2015).

1.3.3.2 Dual task protocol

The so-called 'dual task' protocol consists of asking a person to execute two tasks simultaneously, mainly a motor task and a concurrent cognitively demanding task. Cognition is the ability to perform high level brain functions such as focusing or dividing attention, problem resolution, verbal communication, planning, organization, etc (Sumnima and Jayashankar Reddy, 2013). Walking under dual task aims at emulating every-day life walking since daily life is made of variable environments and social interactions which oblige to perform cognitive tasks while walking in the real world (Schaefer, 2014). Cognitive-motor interferences (CMI) induce a decrease in performances when executing a motor and a cognitive task simultaneously. In accordance with the ICF (WHO), there are good arguments to say that it is one of the disruptive factors playing a role in

the divergence between level of functioning in a standardized environment (defined as "capacity") and the level of functioning in a daily-life environment (defined as "performance") (World Health Organization, 2002). CMI can be assessed by the well established dual-task protocol.

The dual-task paradigm has shown its relevance for the assessment of the automaticity of a motor task: when a motor task is sufficiently acquired, little attentional resource is needed to perform it, whereas when a motor task is not automated enough, a large amount of attentional resource is required and insufficient resources are left to maintain good performance when performing a second concurrent task (Al-Yahya et al., 2011). Although gait as long been considered as an automatic motor task, it has recently been evidenced that gait control requires high-order cognitive systems (Al-Yahya et al., 2011).

The dual-task paradigm has widely been studied in the elderly population, patients with acquired brain damage (e.g. stroke) or people with PD to understand the link between loss of motor and cognitive functions and the risk of fall (Houwink et al., 2011; Montero-Odasso et al., 2012). Walking performances decrease during dual-tasking: decreased velocity, decreased cadence, decreased stride length, increased stride time and its variability (Al-Yahya et al., 2011). The walking speed has actually been shown as a sensitive outcome to distinguish healthy people and those with cognitive impairments (Maquet et al., 2010). New insights on the relevance to use the dual-task protocol for young patients with neurological disorders, like children with CP, needs to be gained (Houwink et al., 2011; Katz-Leurer et al., 2014). Given the coexistence of motor and cognitive disorders in children with CP, we can postulate that they would experience greater CMI than children with TD.

1.3.3.3 Leaving the laboratory

To reflect walking habits, i.e. walking performance, what best than assessing gait in a real life context? The technology advances of the last two decades have permitted miniaturization of electronic devices, increase in robustness, memory and power autonomy as well as decrease in cost (Tao et al., 2012). Therefore, new tools based on wearable sensors have recently been developed to carry out-of-laboratory gait assessments. Light-weight sensors are more and more appropriate to be worn by patients without interfering with their normal movements (Najafi et al., 2009). The next paragraphs introduce existing devices for this purpose, and an exhaustive review of the literature is documented in Chapter 3 to understand what are the technically validated methods to perform gait analysis with wearable sensors.

The most common sensors implemented for measuring gait and physical activity are Inertial Measurement Units (IMU), combining accelerometers and gyroscopes. They are particularly used in the motion analysis field because they enable the measurement of the human body orientation. An accelerometer measures acceleration and inclination (gravity effect) so it can be used to detect known acceleration patterns of specific static postures and dynamic activities (Nez et al., 2016). A gyroscope measures angular velocities which can be used for the estimation of orientation change. Eventually, by integrating the accelerometer and gyroscope signals, it is possible to obtain information about linear and angular displacements. In addition to IMUs, magnetometers, barometers, force sensors and Global Navigation Satellite System (GNSS) receivers can be used to record other relevant data during gait.
As compared to the huge number of studies published in the field of movement analysis using IMUs, the CP population was by far left aside. Table 4 reports the main studies found in the literature until mid April 2019 in three relevant databases (Pubmed, Web of science and Embase), according to the following key words: "cerebral palsy" AND ("IMU" OR 'inertial sensor"). A total of 74 references were selected, including abstracts (i.e. conference communications only). This review did not intend to be exhaustive but was devised to understand the principal trends.

Table 4 - List of references from the literature dealing with the use of IMU in the CP population

Domain	**Main topic**	**References**
Physical activity	Physical activity levels	(Bania et al., 2013, 2014; Clanchy et al., 2009, 2011; Claridge et al., 2017; Gorter et al., 2012; Jner et al., 2014; Johnson et al., 2012; Keawutan et al., 2017; Kelly et al., 2016; Lampe et al., 2013; Maalen-Johansen et al., 2016; Maher et al., 2010; Maltais et al., 2005; Mitchell et al., 2015b, 2015a, 2014; O'Neil et al., 2016, 2014; Pontén, 2013; Rabani et al., 2014; Ryan et al., 2013b, 2013a, 2015; J.M. Ryan et al., 2014; Jennifer M Ryan et al., 2014; Trost et al., 2016)
Gait	Gait detection	(Abaid et al., 2013; Ahmadi et al., 2018)
	Step counting	(Apkon et al., 2014; Bagley et al., 2010; Bjornson and Zhou, 2016; Bjornson et al., 2014; Christensen et al., 2017; Ishikawa et al., 2013; Khan and Biddiss, 2017; Kuo et al., 2009; Maher et al., 2013, 2010; O'neil et al., 2013; Stevens et al., 2017)
	Events detection	(Bruening and Ridge, 2014; Gouwanda, 2013; Taborri et al., 2015)
	Spatiotemporal parameter	(Brégou Bourgeois et al., 2014; Mackey et al., 2008; Manikowska et al., 2013; Mutoh et al., 2016, 2018; Pimentel et al., 2017; Zollinger et al., 2016)
	Kinematics	(Cutti et al., 2010)
	Kinetics-related parameters	(Degache et al., 2014) (abstract)
	Center of mass displacement	(Zollinger et al., 2016)
	Entropy	(Piitulainen et al., 2018) (abstract)
	Body acceleration	(Chen et al., 2017)
	Gait variability	(Børseth-Vassend et al., 2017; Saether et al., 2014)
	Gait symmetry	(Gouwanda and Gopalai, 2015; Mutoh et al., 2019; Saether et al., 2014; Wolff et al., 2018)
	Gait coordination (phase portrait)	(Carollo et al., 2012)
	Gait stability	(Iosa et al., 2018, 2013, 2011; Schulleri et al., 2017; Summa et al., 2016)
Others	Early detection of CP	(Heinze et al., 2010)
	Falls detection	(Smith and Bagley, 2010)
	Upper-limbs	(Li et al., 2017; Newman et al., 2017)
	Game for rehabilitation	(Khan and Biddiss, 2017; Molina et al., 2017)
	Balance (posture)	(Kim et al., 2018; Saether et al., 2015)

It has to be pointed out that more than 30% of the studies using IMUs in CP were interested in physical activity monitoring. This trend came from the large accessibility (low cost and easy-to-use) of the device they used (ActiGraph, USA) which embeds a 3 axis accelerometer. Accelerometer data is transformed into 'activity

counts' which determines physical activity states (from sedentary to vigorous) from empirically determined cut-points. Besides its turnkey advantage, ActiGraph device has the major inconvenience of providing results that are poorly linked with a real clinical meaning (Bjornson, 2019). Moreover, about 15% of the existing literature relates step counting, using mostly pedometers or stepwatches. Almost all remaining studies exploited raw accelerometer and gyroscope data to compute gait features such as variability (Børseth-Vassend et al., 2017; Saether et al., 2014), symmetry (Gouwanda and Gopalai, 2015; Mutoh et al., 2019; Saether et al., 2014; Wolff et al., 2018), coordination (Carollo et al., 2012), stability (Iosa et al., 2018, 2013, 2011; Schulleri et al., 2017; Summa et al., 2016), entropy (Piitulainen et al., 2018), etc. which are not commonly used in the medical practices due to their innovative nature, thus are difficult to integrate within the clinical care process. Among studies using spatiotemporal parameters of gait, only one showed results of accuracy of their system in the CP population (Brégou Bourgeois et al., 2014) (Chapter 3 gives more details). There is indeed a lack of a validated system for such clinical and meaningful parameters.
Inertial sensors prove to be relevant to measure gait features outside of the laboratory, but still need to be further explored to provide accurate and clinically meaningful parameters. Moreover, a recent systematic review of the literature has drawn attention to the lack of studies assessing the feasibility of quantifying gait of children with CP in real-world environments, only 3 articles met their inclusion criteria while all other studies performed their analysis in clinical settings (Rozin Kleiner et al., 2019).

Complementary to inertial sensors, other possible equipment can be used to monitor or analyze daily activity. Pressure insoles have recently shown their relevance in measuring loads under the subjects' foot (Moufawad El Achkar et al., 2016), through piezo-resistive sensors, e.g. force-sensing resistors (FSRs), or capacitive sensors (Crea et al., 2014). Depending on the number of sensors, instrumented insoles can either be used for activity recognition and general gait characterization, stride counting (Truong et al., 2016) or for a precise representation of the pressure distribution under each foot (Crea et al., 2014). Pressure-sensitive insoles can be used in addition to accelerometer and gyroscope on the foot for a more complete gait analysis (Bamberg et al., 2008). In children with CP, plantar pressure data has been used to study the link between changing dynamics during stance phase and the level of impairment of hemiplegic children (Femery et al., 2002; Strohrmann et al., 2013).

Even more possibilities have been developed with E-textiles that combine several wearable sensors such as IMU, electromyography and electrocardiography sensors and/or goniometers (1-degree-of-freedom device for measuring angles) (Patel et al., 2012). Complete 'smart textiles', as reported in this review (Mečņika et al., 2014), including innumerable various technologies to sense every biologic feature from a simple clothe, are still in the stage of prototyping and are very costly, but could be a solution for future gait monitoring in a daily life setting.

A torrent of different solutions is nowadays expanding particularly thanks to the telecommunication field with the development of mobile phone applications and small wearable devices to monitor and improve consumer's health and sports performance. There is a great potential for new sensors on the market that enable activity monitoring and simple movement quantification with affordable prices. Nevertheless, until now these commercial devices and mobile applications have not been tested against a reference to ensure their validation, and their application in healthcare has not yet been established (Del Din et al., 2016b). Indeed, in a review of consumer wearable equipment and mobile applications, Peake et al. demonstrated that only 5% of the technologies were formally validated (Peake et al., 2018). Furthermore, poor accuracy of such devices for pathological movement monitoring has been evidenced (Feehan et al., 2018). Most studies, when existing,

where conducted in laboratory rather than natural settings (Shin et al., 2019). Commercial wearable trackers of activity need to be validated to be used in a clinical context, such as gait analysis of children with CP. Finally, a major drawback with this type of equipment is the non-access to raw data.
Hence, reliable researches turn to the use of IMUs. A review of the methods to compute relevant gait parameters is provided in Chapter 3.

1.4 Thesis objectives and outline

1.4.1 Objective

The natural course of CP can be modulated by various treatments and therapies, aiming at promoting participation in society and general quality of life (Graham et al., 2019). These therapeutic choices depend on the level of impairments and the etiology, so are proper to each individual given the high heterogeneity of CP profiles. Choices are nowadays mostly decided on the basis of the assessments performed in clinical settings. However, it is not clear whether gait assessments in clinics are representative of the daily life behaviors. In the framework of the WHO, what an individual can do in a standardized environment ('capacity') and what he does in his habitual environment ('performance') are two dissociated concepts, and cannot be collected in a single assessment. Along the same line, a majority of existing studies highlight that patients with CP with similar levels of capacity have different levels of performance. The limitation of these findings is the subjectivity of the results, since their conclusions were mainly built on questionnaires. Hence, there is a lack of objective information in order to make sensible and relevant comparisons.
Considering the progress in the design of wearable sensors, notably inertial sensors, being more and more powerful and miniaturized, great enthusiasm recently arose for ambulatory monitoring. Inertial sensors have indeed already shown high potential to perform gait assessment. Testing them in natural settings for a pathological population such as children with CP remains to be achieved, and currently constitutes a great challenge.

This thesis was conceived to address these issues. The primary objective was to bridge the gap between the laboratory and real life in this population of children with CP, by comparing their gait capacity and gait performance characteristics. The parallel was drawn between children with CP and children with TD. Two main specific objectives were established for this purpose:

i. To propose a tool for gait assessments in daily life, based on existing methods, fitting the specific gait deviations of children with CP. This technical objective intended to address the question '*How to fill the knowledge gap about gait performance?*'
ii. To compare gait parameters between standardized and unsupervised walking in order to objectively quantify the differences between gait capacity and performance. And to examine the divergences between children with CP and children with TD. This clinical objective intended to address the question '*How long and how strong is the link between gait capacity and gait performance?*'

The clinical goal adopted a progressive approach, starting with the comparison between standardized gait and gait under challenging situations, such as dual tasks, in the laboratory, and ending with the actual comparison between standardized gait and gait in real life settings.

Eventually, bridging the gap between capacity and performance in children with CP aimed at bringing new insights into how much confidence the clinicians can have in standardized measures, with regard to their patients' everyday-life behavior when devising a treatment strategy. Moreover, given the high heterogeneity

of this population, the integration of performance assessments into the clinical care process would ultimately contribute to favor more personalized and tailored treatment and therapies.

1.4.2 Outline

This thesis is organized in 9 chapters, forming 4 main parts: an introductory, a technical, a clinical and a closure part. A brief description of each chapter is given below and a graphical summary is presented in Figure 10. The first part, including 3 chapters, aims at introducing the clinical (Chapter 1) and technical (Chapters 2 & 3) context of this thesis. The second embraces 2 chapters and reveals the technical results. The third reports the clinical results, and covers 3 chapters. The last part draws general conclusions of this thesis, enriched by some limits and perspectives of the work. Each chapter is organized with an abstract, several sections and a conclusion.

Part I – INTRODUCTION

Chapter 1 introduces the clinical background of gait analysis in children with CP, and briefly describes existing solutions to overcome the major drawbacks of CGA regarding WHO's definitions. This introduction leads to the objectives of the thesis.

Chapter 2 gives more technical information regarding conventional gait assessments in laboratory. It details the equipment and methods for CGA. This chapter serves also as an introduction to the conventions used in gait analysis.

Chapter 3 reports the technical solutions for gait assessments in real life through wearable sensors. This chapter is in the form of a literature review, describing the existing methods to compute spatiotemporal parameters.

Part II – TECHNICAL STUDIES

Chapter 4 gives the results of a study comparing the three most relevant sensor configurations for the computation of spatiotemporal parameters in children with CP. This chapter drives the choice of the wearable solution that is used in the thesis, on the basis of accuracy and precision of the three configurations as compared to the clinical reference and the patients' acceptance.

Chapter 5 presents a method to improve gait detection in real-life settings based on a personalization set-up with laboratory assessments. A comparison between existing and personalized approaches is presented, in terms of sensitivity, specificity, accuracy and precision for walking bout detection, during a semi-standardized route outside of the laboratory.

Part III – CLINICAL STUDIES

Chapter 6 deals with the first clinical comparison between standardized gait and more challenging gait assessed in the laboratory, reflecting a situation closer to a real life situation. The effect of dual tasks on gait in children with CP and children with TD is discussed.

Chapter 7 presents the comparison between supervised and unsupervised gait, on the basis of a unique metric, which is a global indicator of the gait function: the walking speed. Gait episodes are detected by the personalized approach proposed in Chapter 5. All detected gait episodes in real life are included in this analysis to represent an overview of the patient's walking habits.

Chapter 8 presents the comparison between supervised and unsupervised gait, focusing on multiple features of the gait function. Gait function is described by multiple gait features belonging to various gait domains (pace, rhythm, variability, symmetry, amplitude, stability, smoothness and coordination) and compared between laboratory and daily life settings. Gait episodes are also detected by the personalized approach

proposed in Chapter 5. However, only gait episodes reflecting the laboratory constraint, i.e. with a travelled distance similar to the walkway length, are included in this analysis.

Part IV – CONCLUSION

Chapter 9 includes the summary of the results of the thesis and underlines the main contributions with regard to existing literature. It also brings discussions linking the different chapters together regarding the technical and clinical aspects. Finally, the limits and perspectives of the thesis are described.

1.4.3 Graphical summary

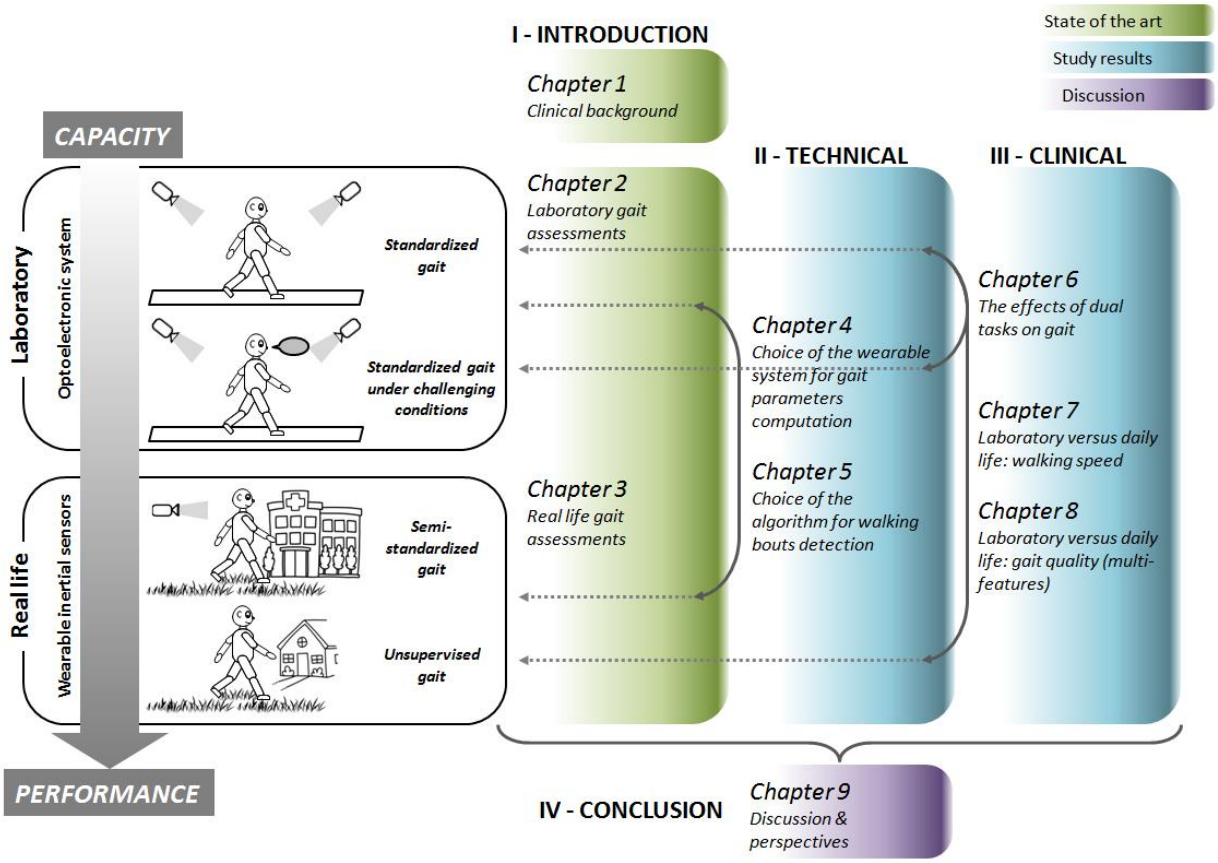


Figure 10 - graphical summary

1.4.4 Overall method

Within this framework, a serie of gait acquisitions in different environments were set up, belonging to two distinct study protocols (two distinct ethical committee agreements) and involving two different groups of children and adolescents with and without CP, as illustrated in Figure 11.

In protocol A, the participants were asked to walk in the laboratory as if they were performing a CGA, at self-selected spontaneous speed, and also at slow and fast speeds, while wearing the standard in-laboratory equipment and wearable equipments. Then, right after the in-laboratory gait measurements, the participants had to leave the laboratory with the wearable equipment for a sequence of semi-standardized daily activities in the hospital surroundings, while the investigator was video filming them. Later on, the participants were asked to wear the wearable equipment in their daily life for three days.

In protocol B, the participants came to the laboratory for gait assessments in simple and dual tasks. For this protocol, only the standard equipment was used.

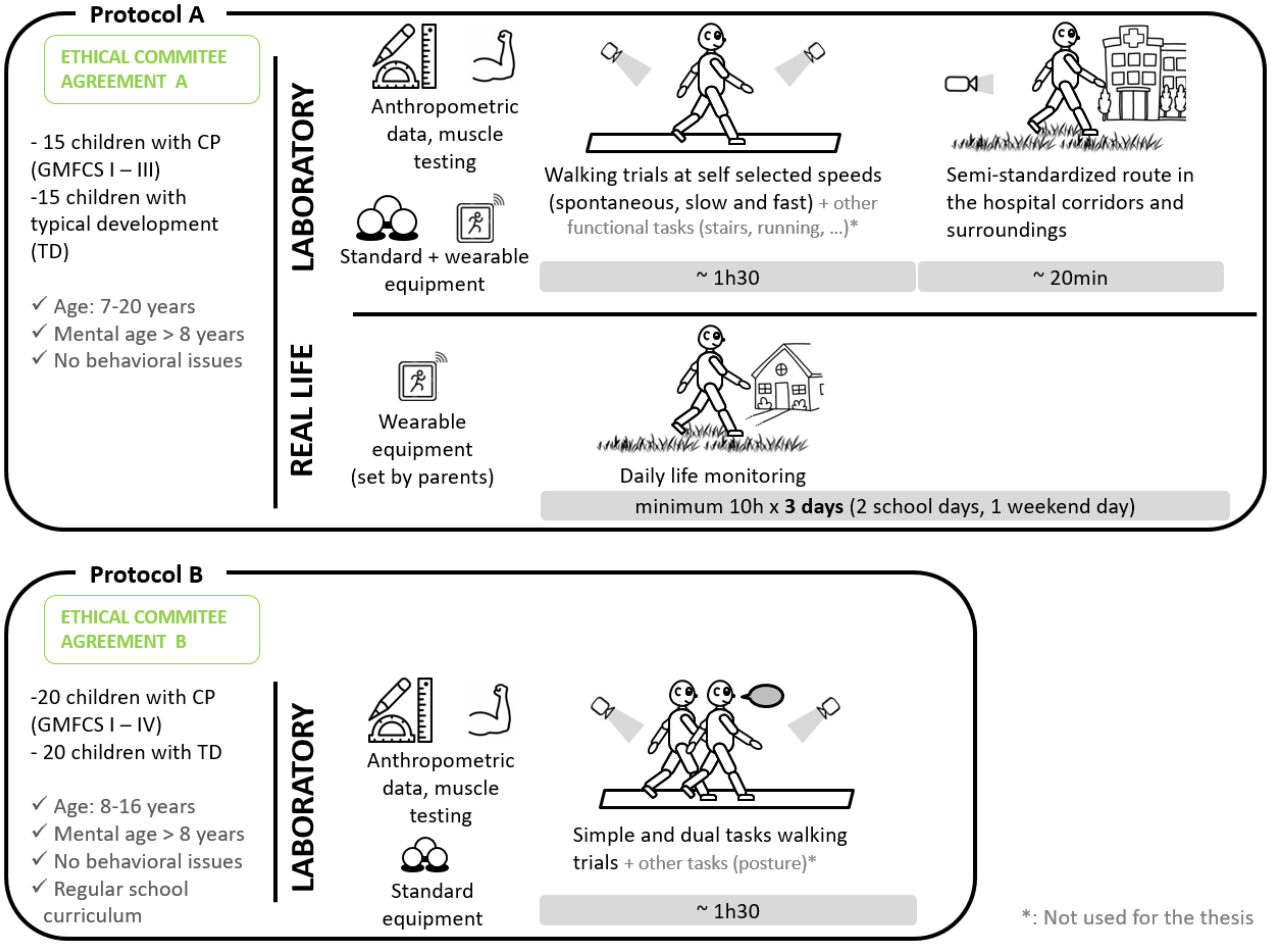


Figure 11 – Overall method of the thesis, including gait assessments in various environment and conditions, belonging to two distinct study protocols (A and B).

Chapter 2 *

Laboratory measurements: the Clinical Gait Analysis – State of the art

Abstract

Ensuring effective and harmonious gait for patients with neuro-musculoskeletal disorders has nowadays become one of the main objectives of clinicians. For this purpose, the patients can perform an assessment of their gait called "Clinical Gait Analysis" (CGA), or "3D gait Analysis" (3DGA). The goal of this clinical examination is to obtain quantitative information on the patient's gait that can be used to better identify and understand his motor disorders. Although this clinical evaluation is not yet standardized among the different laboratories around the world, common practices can be depicted. The objective of this chapter is to give an overview of these practices, i.e. the conventional definitions, the procedures, the biomechanical principles, the equipment needed, and the steps until clinical recommendations. The main limitations and the controversy associated with the clinical efficacy of this examination are also presented at the end of this chapter.

* Chapter adapted from the following article:
Carcreff L., Bonnefoy-Mazure A., De Coulon G., Armand S. "Analyse quantifiée de la marche" Movement & Sport Sciences – Science & Motricité, 2016, vol. 3, num. 93, p.7-21. doi: 10.1051/sm/2015033 – with permissions of all co-authors
My contribution: Investigation, visualization, writing - original draft preparation, writing-review & editing

2.1 Brief history

Even if Aristotle (384-322 BC) was the first to observe human gait, the scientific bases of movement analysis, as it is realized today, were not set before the XVIth century (with Galileo, Newton or Descartes). The advent of photographical techniques around the middle of the 19th century introduced by É.J. Marey (1830-1904) and E.J. Muybridge (1830-1904) considerably helped the first two-dimensional precise description of movements (Baker, 2007). Then, the first tools of three-dimensional measurement systems (Sutherland, 2002), force plates (Sutherland, 2005) and electromyography (Sutherland, 2001) were born between the XIXth century and the XXth, until the advent of modern computers which has revolutionized the world of motion analysis (Baker, 2007). Tools became more efficient so the number of computable parameters increased significantly. First, the displacement of the center of gravity and the spatiotemporal parameters of gait were analyzed. Then, linear displacements of each segment and angular displacements of each joint were described. And finally, kinetics, muscular activity or plantar pressures were added.

2.2 Conventions

2.2.1 Gait cycle

By convention, gait is divided into gait cycles to ease its description. A gait cycle, also called 'stride', is defined as the element starting from the initial foot contact with the ground until the subsequent contact of the same foot (Armand et al., 2016). The key events to characterize a gait cycle are the moments when the foot contacts the ground, called "foot strikes" (FS), or "initial contacts", and the moment when the foot leaves the ground, called "foot off" (FO) or "terminal contact", as illustrated in Figure 12.

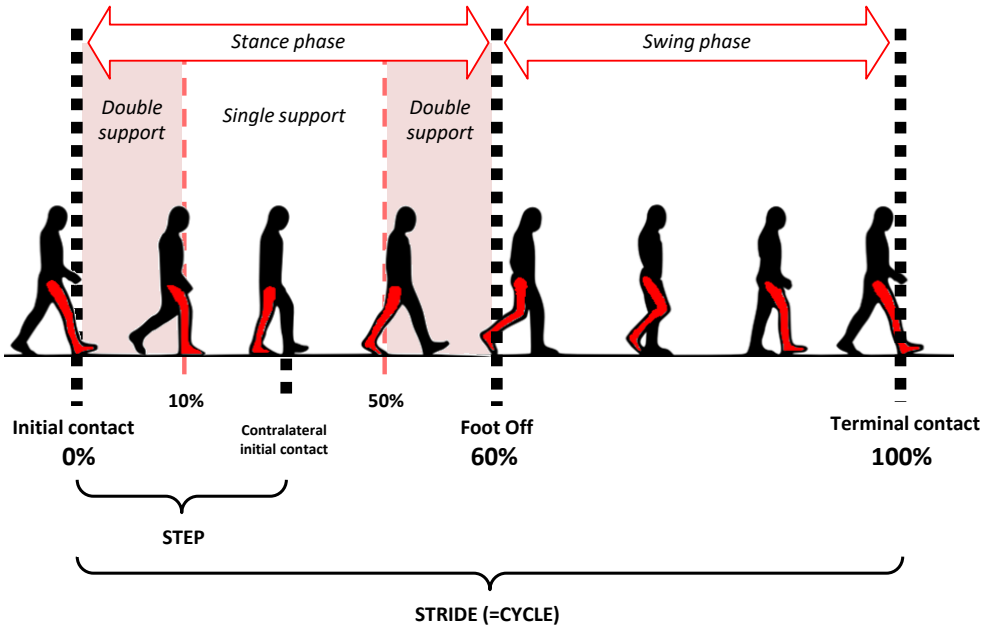


Illustration adapted from (Carcreff et al., 2016a)

Figure 12 - A gait cycle and its phase division

A step is defined between the right and left foot contacts. Two phases are defined from these events: the stance phase (foot in contact with the ground) which contributes to about 60% of the gait cycle and the swing phase (no contact with the ground) corresponding to the remaining 40%, for an asymptomatic person at a comfortable speed. Also, the double support phases are characterized by both feet in contact with the ground, accounting

for approximately 20% of the gait cycle (Figure 12). Other temporal parameters related to the gait events are presented in the following section.

2.2.2 Anatomical planes

Gait analysis is based on the principles of biomechanics where the body is considered as a rigid poly-articulated mechanical object, supposed non-deformable, which can be decomposed into several segments. A coordinate system is assigned to each body segment and the description of the orientations of a system relative to another, or relative to the global coordinate system, constitutes the principle of movement analysis. Three anatomical planes can be defined from the coordinate system: the sagittal containing the upward and forward axes (generally describing flexion/extension motion), the frontal or coronal plane containing the upward and lateral axes (abduction/adduction) and the transverse plane containing the forward and the lateral axes (internal/external rotation) (Figure 13) (Baker, 2013).

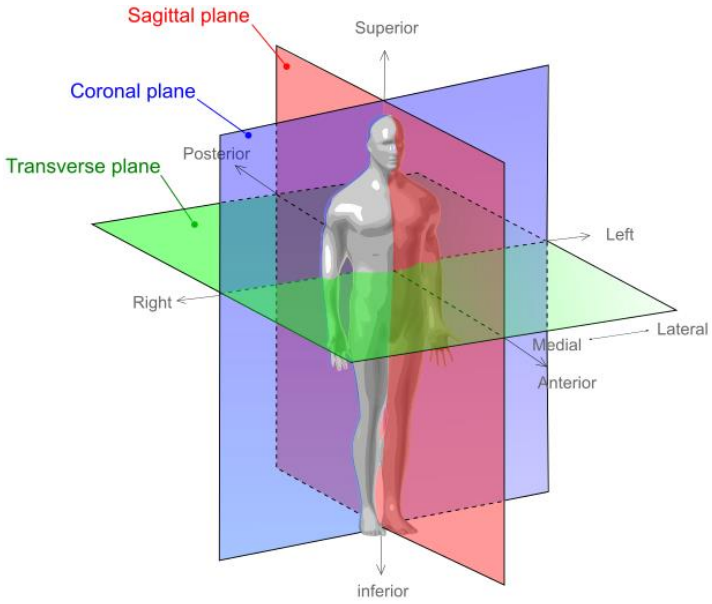


Image Adapted from a CC BY 3.0 image (https://creativecommons.org/licenses/by/3.0).

Figure 13 - Anatomical planes and axes

2.3 Conventional clinical gait analysis

2.3.1 Physical examination

The physical examination, carried out by a physiotherapist or a specialized doctor, is an inspection of the human body in its entirety with a precise evaluation of the musculoskeletal system of the lower limbs. Possible deficits of motor control, muscular weaknesses, retractions, spasticity, bone deformities, and pain are evaluated in detail.

2.3.1.1 Anthropometric measurements

The weight and height of the patient, as well as lower limb lengths and widths, are measured at the beginning of the clinical examination. This helps highlighting possible leg length discrepancy. In addition, these measurements are used for the estimation of joint centers and inertial parameters for kinematic and kinetic data calculation algorithms.

2.3.1.2 Measurements of the articular amplitudes

The maximum passive mobility of each joint is measured with a goniometer (Viehweger et al., 2007). Muscle retractions or laxities can be detected by comparing the patient's ranges of motion with normal amplitudes. It should be noted that goniometers have rather low precision (inter-examiner and inter-session error can reach 15°) (Mcdowell et al., 2000).

2.3.1.3 Muscle strength and selectivity assessment

Muscle strength and selectivity are evaluated using clinical scales (Florence et al., 1992; Fowler et al., 2009) while the patient is asked to perform specific resistance movements against the evaluator. A single muscle or muscle group should be recruited (selectivity). The understanding of the exercises is not always straightforward, especially for a young child (under 5) or a patient with intellectual disabilities.

2.3.1.4 Assessment of muscle tone

Ashworth (5-point scale) (Bohannon and Smith, 1987) and Tardieu (report of threshold angles where the muscle reacts to the stretch, at several predefined velocities) (Gracies et al., 2010) scales are the reference tools for clinical assessment of spasticity. The reproducibility of these scores is low (e.g. only 42.5% of concordance found between the scores attributed to one muscle by different experimenters (Blackburn et al., 2002)).

2.3.2 Gait assessments

2.3.2.1 Material and outcomes

Figure 14 illustrates the equipment used in gait analysis laboratories, and a description of each equipment is given in this section.

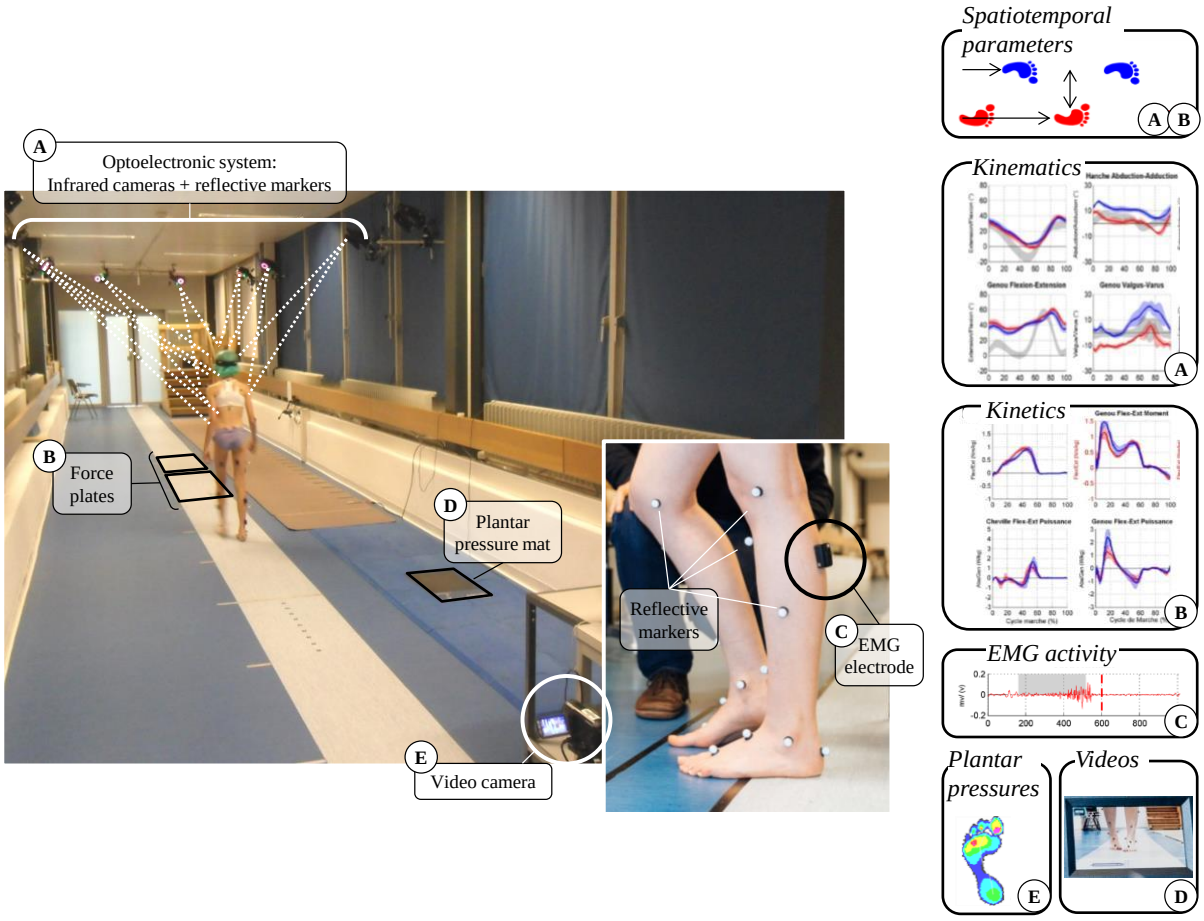


Figure 14 - Material used in gait analysis and associated outcomes

Gait analysis laboratories contain a straight walkway of about 10 to 20 meters, however in the case of a lack of space, walking tests can also be performed on a treadmill. However, no unanimous consensus exists on whether treadmill accurately reflects overground natural walking (Martin and Li, 2017). Indeed, ground forces, compensatory movements, muscle activation, plantar pressures and metabolic cost were found different between treadmill and overground walking at the same speed, in various populations (Martin and Li, 2017; Parvataneni et al., 2009; Rozumalski et al., 2015; Van Der Krogt et al., 2015; Wearing et al., 2013).

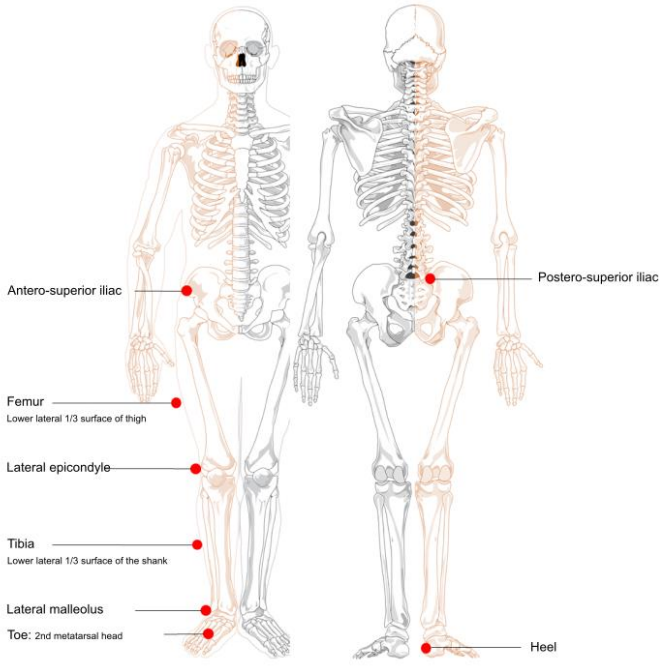
Video cameras for an overview of the gait pattern

Video cameras are essential to qualitatively evaluate the movement and have a first overview of the overall gait pattern of the patient, to detect unquantifiable alterations or to evaluate the progress after treatment. Several video cameras are thus disposed in the laboratory to record different planes (sagittal, frontal and transverse planes).

Optoelectronic system for kinematic data

Kinematics is the description of linear and angular movements of the body without taking the forces (internal and external) inducing the movement into account. Optoelectronic systems, also called stereophotogrammetric systems (Cappozzo et al., 2005), are currently the reference for gait kinematics computation. The principle is to model body segments using markers placed on the skin at specific anatomical landmarks. The 3D position (x, y, z) of a marker is determined by the intersection of infrared light rays emitted by at least 2 calibrated cameras. Several infrared cameras are necessary to track the whole body, and during several gait cycles. From 8 to 12 cameras are generally used for CGA (Baker, 2013).

In 3D, a segment is defined by 3 non-collinear points (triangle) to characterize its position and orientation, meaning that at least 3 markers are needed to determine the frame of a body segment. Marker placement is defined by a protocol depending on the biomechanical model used to calculate kinematics and kinetics thereafter. Most CGA laboratories use variants of the 'conventional gait model' (Davis et al., 1991; Kadaba et al., 2014), which are included in most commercialized capture systems. Figure 15 shows an example of placement of markers on the lower limbs.

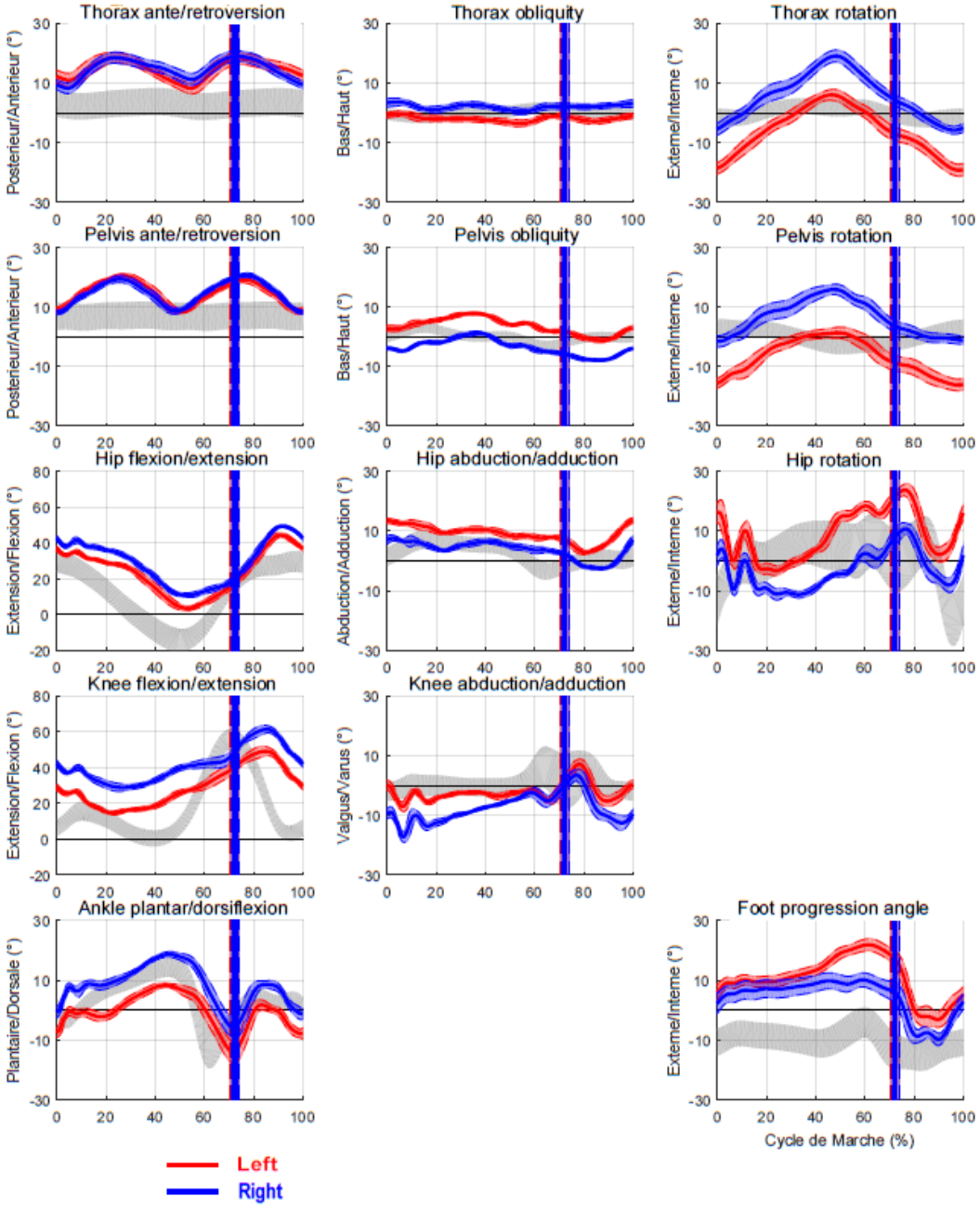


Adapted from (Carcreff et al., 2016a)

Figure 15 - Marker placement according to a conventional gait model

From the anatomical frames, translations and rotations of the segments, and eventually the joint angles, can be computed through direct or inverse kinematics ("multi-body optimization") (Kainz et al., 2017). For each joint, conventions exist for the local axis system in each articulating segment or bone, provided by the International Society of Biomechanics (Wu et al., 2005, 2002).

The 3 lower-limbs joints (ankle, knee, hip), the pelvis and the trunk kinematics are mostly studied according to the 3 anatomical planes (Figure 16). The purpose is to detect eventual decreased or increased range of motion, asymmetry or abnormal movement pattern, detected through the abnormal shape of the curves. The reproducibility of the patient's gait can be assessed by superimposing the curves of all the recorded gait cycles. Usually, kinematic curves are represented as mean and standard deviation, or as the representative cycle (Schweizer et al., 2012), next to 'normality' curves, with regard to the gait cycle (in %).

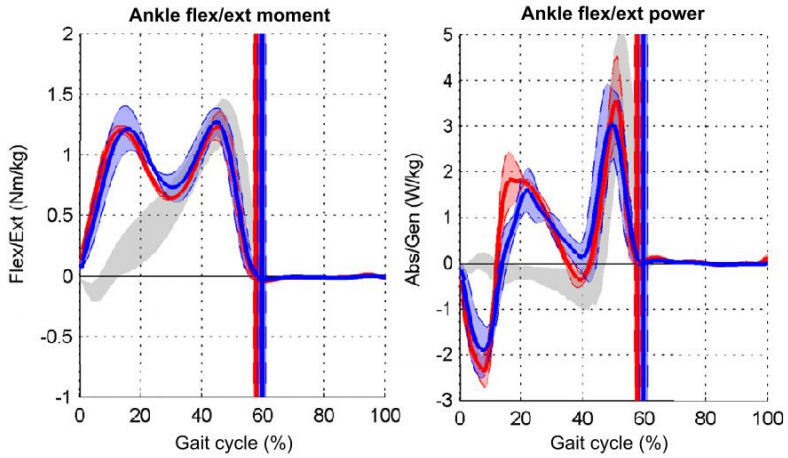


In red (left) and blue (right): mean and standard deviation for a child with CP; in gray: normal gait area; vertical lines: foot offs.

Figure 16 - Kinematic graphs of the thorax, pelvis and lower limb joints in the sagittal, frontal and transverse planes of a child with CP in comparison with normal pattern

Force plates and optoelectronic system for kinetic data

Kinetics describes the forces and powers involved during walking. Force plates are dynamometric instruments that measure forces and moments in three dimensions. The force plates' sensors can be of different types: the best known are the strain gauges and the piezoelectric sensors. This tool is embedded in the middle of the walkway. Force plate data coupled with the kinematic and anthropometric data allow, by a method called "inverse dynamics", to calculate the force, net moments and powers at each articulation. The moment reflects the ability of a force to rotate a segment around a rotation axis. The net moments result from muscular and non-muscular actions around an articulation causing the movement (Bonnefoy-Mazure et al., 2015; Derrick et al., 2019). Moments can be expressed as external (related to external forces applied to the joint such as body weight or ground reaction force) or internal (interpreted as forces exerted by muscles or other structures around the joints in response to external forces) moments. Joint power is the product of the net muscle moment and angular velocity (Winter, 2009), indicating the type of contraction of the muscular group (concentric during energy generation, eccentric during energy absorption, isometric when the power is zero). The study of moments and power can be done in the sagittal, frontal and transverse planes; the sagittal (Figure 17) and frontal planes are mainly studied in the clinic.



In red (left) and blue (right): mean and standard deviation for a child with CP; in gray: normal gait area; vertical lines: foot offs.

Figure 17 - Kinetic graphs of the ankle of a child with CP in comparison with normal pattern

Instrumented mat for spatiotemporal parameters

The spatiotemporal parameters are global parameters describing the organization of the movement in time and space (Armand et al., 2014). The main parameters are the velocity, the cadence, the cycle time (also called stride time), the stride length, the step time, the step length, the step width, the stance/swing phase duration and the double support (Table 5). All these parameters can be used to objectively identify asymmetry, reproducibility, and efficacy of gait. They can be exploited to easily evaluate the efficiency of a treatment.

Large instrumented pressure walkway (such as GAITRite, USA or Zeno Walkway, USA) or optical detection systems (like Optogait, Italy) can be used, and are actually considered as the standard, for spatiotemporal parameters computation. These instrumented mats have the advantage not to necessitate any specific equipment on the patient, to record more gait cycles than during optoelectronic recordings, and to be fast for data processing. However, in most gait analysis laboratories, spatiotemporal parameters are determined using the above-mentioned optoelectronic system coupled with force plates to combine both spatiotemporal parameters and kinematics recording at the same time.

Table 5 - Spatiotemporal parameters of gait (definitions, normal values, common units)

Parameters	Definition	Normal value	Unit
Temporal			
Stride time (GCT)	Time between two consecutive foot strikes of the same foot	0.9-1.1	sec
Step time	Time between right and left foot strikes	0.45-0.55	sec
Cadence	Number of steps per unit of time	100-130	step/min
Stance time	Time between foot strike and foot off	55 – 65	% of GCT
Swing phase	Time between foot and foot strike	35 - 45	% of GCT
Double support	Time between foot strike and foot of a foot + time between foot strike and foot off of the other foot	10-20	% of GCT
Spatial			
Stride length	Anteroposterior distance between two consecutive foot strikes of the same foot (generally between heel positions)	1.4-1.6	m
Step length	Anteroposterior distance between right and left foot strikes (generally between heel positions)	0.65-0.80	m
Step width	Mediolateral distance between right and left foot strikes (generally between heel positions)	0.05-0.15	m
Spatio-temporal			
Stride velocity (or walking speed)	Anteroposterior distance traveled per unit of time temps (generally stride length/stride time)	1.1-1.6	m/s

GCT: Gait cycle time

The normal values are based on the Willy Taillard laboratory of kinesiology's database of healthy subjects

Gait Scores

Various gait scores or gait indexes have been introduced to summarize gait quality (distance with a norm) in one single value. These scores are calculated from spatio-temporal and/or kinematic parameters, and are based on the comparison with normative values. The most used scores are the Gillette Gait Index (GGI) (Schutte et al., 2000), the Gait Deviation Index (GDI) (Schwartz and Rozumalski, 2008), and the Gait Profile Score (GPS) (Baker et al., 2009). The GGI is a measure of the difference (mean square of the distance) between a patient's gait and the mean pattern of healthy subjects, which computation is based on 16 uncorrelated (through multivariate statistics) discrete spatiotemporal and kinematic parameters (Baker, 2013; Schutte et al., 2000). The GDI measures the logarithmic-transformed Euclidean difference between gait vectors composed of 9 kinematic parameters (pelvis, hip in the 3 planes, knee and anke in the sagittal plane, and the foot progression angle) across the gait cycle of the patient and typically developing children (Baker, 2013; Schwartz and Rozumalski, 2008). The GPS is the measure of the direct RMS difference between an individual's gait data and the average data from typically developing children from the same 9 kinematic parameters (Baker, 2013; Baker et al., 2009). These scores are particularly useful to follow the global evolution of a patient in time, and are widely used in research.

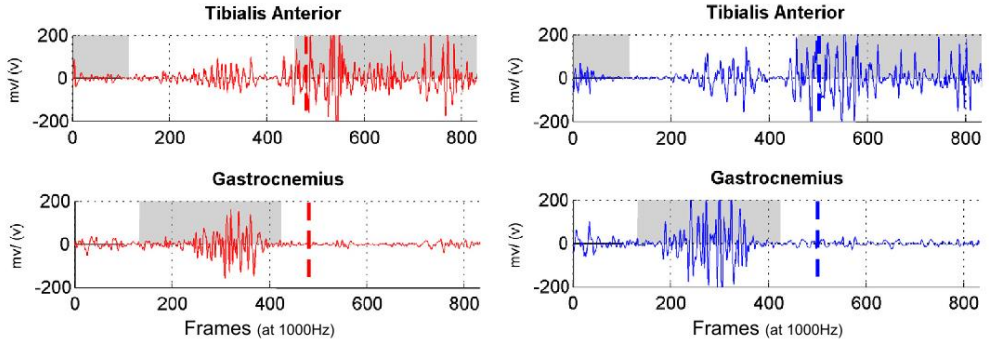
Electromyography electrodes for data on muscle activity

Electromyography (EMG) is a measure of the electrical activity of the neuromuscular system occurring during the movement. Indeed, muscle fibers are controlled by the nervous system via electrical impulses called 'action

potentials'. The main goal of EMG in CGA is to determine the timing of muscular activations (determined by a change in signal amplitude) during gait.

EMG recording is done via electrodes which detect the sum of the action potentials driven in each muscle fibers of the muscle of interest. EMG electrodes can be placed on the surface of the muscle (surface EMG) or implanted directly into the muscle transcutaneously (fine wire EMG). The advantage of the latter is that they can measure deep muscles but only measure one or a few muscle fibers. Surface EMGs are generally preferred since they are noninvasive. The precise location of the electrodes is needed, thus recommendations, like the SENIAM's (Surface EMG for Non-Invasive Assessment of Muscles, www.seniam.org) or references in the literature (Blanc, 2010) are followed to record the best signals. They must be placed parallel to the muscle fibers of the studied muscle.

The EMG signals can be represented after different types of signal processing (filtered, smoothed, rectified) (Davis, 1997) during the gait cycle (Figure 18). Timing and intensity of activation during a gait cycle are visually observed against reference data to identify possible irregularities in contractions, co-contractions or even spasticity (increased muscle tonus) (Sutherland, 2001). The amplitude of the EMG is indicative of the extent of muscular activity but is very variable depending on the muscle studied, or the skin impedance. Therefore, EMG amplitude cannot be directly interpreted as muscle strength. The timing of activation between two muscles, e.g. pair of co-activated muscles, can be compared by cross-correlation (Nelson-Wong and Callaghan, 2010).



Red (left) and blue (right): EMG signal of a child with CP; gray: normal EMG activation area; vertical dashed lines: foot offs.

Figure 18 – Electromyography graphs of gastrocnemius and tibialis anterior muscles of a child with CP during one gait cycle

Plantar pressures mat to study the pressures under the feet

The measurement of plantar pressure, or baropodometry, gives an instantaneous indication of the pressure distribution under the foot. It is a set of sensors distributed evenly in a treadmill. This evaluation is generally done in a non-concomitant way with the kinematic, kinetic and EMG analysis because the pressure mat can hardly be embedded in the walkway and non-visible to the patients.

Plantar pressures data are represented as color-scaled isobars allowing a good visualization of the pressure distribution under the feet (Figure 19). The trajectory of the center of pressure and the distribution of the pressures under the foot during the step course are especially studied. Overloads or underloads can thus be detected. For instance, this information can highlight overloaded areas of the foot and prevent the damage before it becomes painful for patients with foot deformities or suffering from a loss of sensitivity.

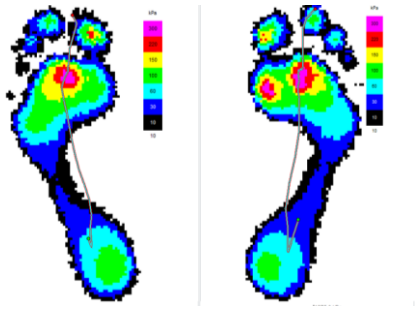


Figure 19 - Isobars with a color-scale representing the pressures under the feet of a child with CP during the gait cycle and lines representing the trajectory of the center of pressures

The measures of energy expenditure

Walking is, like any physical activity, an exercise that requires energy. The synthesis of muscle-usable energy molecules (ATP) is a process that consumes oxygen and produces heat and carbon dioxide. Energy expenditure can be estimated by measuring oxygen consumption (by pneumotachometer or spirometers), heat production (by thermometer) or heart rate (by heart rate monitor). The evaluation of energy expenditure allows appreciating the efficiency of a patient's walk (Robert et al., 1999).

2.3.2.2 Conduct of an examination

Before each visit, calibration of the optoelectronic system, i.e. determining the position and orientation of the cameras between themselves as well as the position and orientation of the force plate(s), is necessary. For this purpose, a calibration wand incorporating reflective markers at known fixed distances one to the others is waved in the laboratory corresponding to the capture volume (Baker, 2013). A capture with a similar calibration wand placed on the force plates allows the former relative camera calibration to be aligned with the global laboratory coordinate system (Baker, 2013).

When the patient comes, first of all, an anamnesis (medical history and history of the disease) is made in order to have good knowledge of the case and the reasons for the examination. The doctor's prescription letter is also of great help to guide the examiners.

Once the patient is equipped with the markers and EMG electrodes, a static recording is generally performed which will later be used to define axes and joint centers and, for some motion analysis systems, to automatically recognize markers by the processing software (auto-labeling). Then, the patient walks barefoot back and forth along the walkway, the number of times necessary to acquire enough valid passages. Valid passages include entire feet on the force plates and a natural walk. The more trials recorded; the better the evaluation of the reproducibility of gait. The number of trials also depends on the patient's ability to walk. For highly affected patients, only one or two trials can be performed. In general, approximately 10 walking cycles are used to characterize a patient’s gait. For the evaluation of plantar pressures, it is also recommended to take at least 3 valid measurements for each foot (foot at the center of the pressure mat).

Depending on the case, some additional recordings can be made. Such as walking with orthosis, running, balance, etc.

2.3.3 Data processing

The first phase of data processing consists of recognizing the markers on the three-dimensional view, and then filling the gaps in marker trajectories resulting from occlusions. The second step is the identification of gait events (FS and FO). Their identification can be done manually, thanks to force plate data or by automatic detection from kinematic data. Commercial or opensource softwares, such as Mokka (Motion Kinematic & Kinetic Analyzer) (Barré and Armand, 2014), allow viewing the 3D reconstruction of the markers and can be used to manually define the event times. Force plate data allow the identification of FS and FO using force

thresholds (Boutaayamou et al., 2014; Veilleux et al., 2016). The inconvenient of using force data only is the need of a large number of trials with entire foot contact on the surface of the platform (Veilleux et al., 2016). Besides, for patients using walking aids or having drag foot, force plate data turns erroneous (Lempereur et al., 2019). For these reasons, multiple algorithms have been developped for the automatic detection of gait events using kinematic data (Boutaayamou et al., 2014; Bruening and Ridge, 2014; Zeni et al., 2008) or combining kinematic and force plate data (Stanhope et al., 1990). More recently, deep learning approaches were developed and prove to out-perform any previously-mentioned kinematic-based models for pathological gaits (Kidzińskiid et al., 2019; Lempereur et al., 2019). Anyway, visual validation of gait events detection is strongly recommended at the end of this data processing step. Low-pass filtering is applied to the marker trajectories and the EMG signal to remove any movement artifacts in the data. Spatio-temporal parameters, joint angles, moments and powers are calculated by commercial software (Vicon, USA or C-Motion, USA), open-source packages (Leboeuf et al., 2019, 2016), or algorithms internally developed, from the marker trajectories, anthropometric data, and force plates data.

2.3.4 Interpretations

A multidisciplinary team consisting of at least one physician and the person who was in charge of the data acquisition is needed to interpret the results. Ideally, a person who regularly follows the patient as a physiotherapist joins the interpretation session. The team reviews all the available data: videos are watched carefully to observe the general way of walking. Gait scores give the team an idea of the patient's general impairment. Spatiotemporal, kinematic, kinetic, EMG and plantar pressure parameters are described in detail. Relationships between the various sources of data (from CGA, but also imaging, physical examination, etc.) are established. The objective is to distinguish between the primary elements of the pathology and the compensatory elements (Davids, 2006; Romkes and Brunner, 2007). Guidelines exist to help the identification of abnormal gait features on the data, the grouping of information, the reporting and the elaboration of recommendations, such as the one of R. Baker with his ‘Impairments Focus Interpretation’ (Baker, 2013). In summary, the heart of CGA data interpretation is linking clinical and biomechanical data to lead to the identification and understanding of a patient's gait disorders. These results are integrated into the patient’s medical file, and sent to the medical doctor or therapist to guide the therapeutic choices.

2.3.5 Limitations

Equipment

First of all, the reconstruction of the markers’ position in three dimensions is closely linked to the accuracy of the equipment. The number of cameras, their resolution, their optical quality or their position in the laboratory play a crucial role. The marker size and the number of cameras will determine the amount of obstruction (marker flickering) that will occur, especially during arm and leg swinging or due to assistive devices (Chiari et al., 2005). Besides, algorithms for marker imaged processing can generate reconstruction error (Chiari et al., 2005). The mean absolute error of the optoelectronic system (Vicon) evaluated with a rigid structure with markers attached at known locations and angles was found less than 2mm and 1.7° in dynamic situations (Di Marco et al., 2017; Merriaux et al., 2017), indicating excellent precision when markers are attached to a rigid body (Colyer et al., 2018). However, the performances decrease when 3D joint center positions are estimated from markers located on the skin (Colyer et al., 2018).

Soft tissue artifact

Soft tissue artifact is the consequence of the movement of the marker relative to the underlying bone due to skin deformation and displacement during walking. It constitutes the most critical source of error in 3D gait

analysis (Baker, 2006; Leardini et al., 2005) affecting different outputs such as kinematics and kinetics. This artifact is highly variable among subjects, tasks and lower limb segments (Barré et al., 2017); being the highest at thigh level given the muscle and fat volumes (Leardini et al., 2005). Several attempts to reduce or compensate these artifacts have been performed such as modeling the skin surface, including joint constraints and using a multi-body kinematics optimization (Camomilla et al., 2017b). The effect of artifact compensation is assessed by comparing kinematic and kinetic data with those computed from pins inserted into bones or by medical imaging techniques (Camomilla et al., 2017b) such as biplane fluoroscopy (Barré et al., 2017, 2013). Consequent errors of soft tissue artifact were reported up to 11° for pelvis angles during hip movements in 3D (Camomilla et al., 2017a), and up to 4.1° for knee angles during gait (Barré et al., 2013). It is worth mentioning that this soft tissue artifact should not be considered as an issue only for optoelectronic systems, since they affect all measurement using devices positioned on the skin (e.g. wearable sensors).

Marker misplacement

Marker placement, through palpation, is a delicate step of CGA since it is necessary to adapt to the morphology of the subject. Although precise recommendations of marker placement exist, experimenters require high expertise to attain good reproducibility. An error in the placement of a marker may distort the results. This difficulty of positioning is encountered especially when placing the markers on an obese person or a patient with significant bone deformities. Markers are fixed on the skin at an a priori known distance from the internal skeleton but in case of misplacement, errors arise directly impacting the estimation of the joint center. Della Croce et al. (2005) reported the hip joint center estimate error to up to 10.5mm. Functional methods have emerged for the localization of this joint center which is particularly difficult to determine (Camomilla et al., 2006; Sangeux et al., 2014). Regression methods were developed and the Harrington's method (Harrington et al., 2007) based on MRI imaging data was found the most reliable and usable for all populations (Sangeux, 2015). A fusion of kinematics and imaging data to improve the determination of joint centers, axis systems and the positioning of markers on anatomical points emerged as well (Assi et al., 2013; Passmore and Sangeux, 2016).

Besides, markerless methods could be a relevant alternative. This approach has been proposed by several researchers: through automatic recognition of the limbs (extraction of the silhouette of the legs) from standard video captures (Parent et al., 1999) or recognition of the movement by a system of Kinect (peripheral developed by Microsoft to control video games by camera, without using a controller) (Pfister et al., 2014). Some systems show good accuracy (2-3°) in estimating sagittal plane angles during gait (Colyer et al., 2018). However, as of today accuracy remains insufficient for clinical use (Colyer et al., 2018; Pfister et al., 2014).

EMG

Regarding EMG, type and placement of the electrodes, the interface between the skin and the electrode (fat, hair, lotion ...) or the presence of adipose tissue between the fibers muscle and the electrode, muscle length and muscle depth can influence the signal quality. In addition, surface electrodes can record the activity of adjacent muscles in addition to the muscle of interest (called 'crosstalk').

Biomechanical models

In addition, one of the fundamental limits of CGA is the use of biomechanical models that are only a simplified representation of the human anatomy. Indeed, the principles are based on rigid and non-deformable segments. For instance, the foot comprises several bones with many degrees of freedom, which move relatively to one another during walking, unlike a rigid solid (Pothrat et al., 2015). Thus, several researchers have developed more adapted models for the study of the foot, considering it as a set of several segments (Carson et al., 2001;

Levinger et al., 2010; Myers et al., 2004; Scott and Winter, 1993). These models are however slightly used in the clinic because of the time required to place all the markers and also due to the difficulty of interpretation.

Dissemination and representativeness

Besides limitations regarding accuracy and reproducibility, CGA has two major issues. The first one is the difficulty of dissemination. Indeed, CGA requires a dedicated laboratory including advanced equipment and also qualified and multidisciplinary personnel, which contribute to its high cost. Even in developed countries, few clinical gait analysis laboratories exist (about 5 in Switzerland, 23 in France, 50 in USA for instance), obliging families with a child with disabilities to travel sometimes far for repetitive CGA during several years of childhood. Even if the prices of such commercial systems decrease regularly due to concurrence, the devices and software packages remain unaffordable for many institutions (costs for a motion capture system between $50'000 and $300'000). Furthermore, more courses are needed to train professionals, especially clinicians and therapists in order to be able to understand the "gait report" which can be lengthy and complex for novices (Simon, 2004). More training would lead to increasing the number of laboratories. Finally, CGA suffers from a lack of standardization. Yet, several organizations like, for example in Europe, the European Society of Motion Analysis in Children and Adults (ESMAC), the Clinical Movement Analysis Society of UK and Ireland (CMAS), the Italian Society of Clinical Movement Analysis (SIAMOC), the Societé Francophone d'Analyse du Mouvement chez l'Enfant et l'Adulte, exist and tend to bring consensual practices regarding laboratory management, instrumental issues, clinical appropriateness, etc. (Benedetti et al., 2017).

The second issue comes down to the drawbacks highlighted in Chapter 1, regarding the lack of representativeness of the measures. As explained, walking in a laboratory surrounded by cameras and caregivers is not likely to reflect the way of walking in daily life. These two concerns are major topics nowadays in the field of gait analysis and they both bring the need for new tools, which would have to be low cost, easy to use, and wearable outside of the laboratory in daily life situations.

2.3.6 Clinical efficacy of CGA in CP – Pros and Cons

2.3.6.1 A great benefit for children with CP

CGA has shown its effectiveness to improve the understanding of motor impairments for patients with orthopeadic troubles (Wren et al., 2011b). Actually, the evaluation of patients with serious gait disorders, like children with CP, has changed dramatically over the past 50 years, thanks to the advent of motion capture laboratories, as reported by Gage J. R., an orthopedic surgeon and strong international advocate of CGA (Gage et al., 2009). Indeed, at the end of the 1970s, a patient was assessed only by reviewing his clinical history and a simple examination including rapid observation of his way of walking and some routine x-rays. Knowledge about locomotor control was precarious at that time (Gage et al., 2009). The surgical procedures were based on empirical methods. Results of the surgery were not always beneficial for the patients, and the surgeons had no way to get feedback on their procedures, so they could not improve their practices. Technological advances of the following years allowed providing motion analysis platforms to the clinics, revolutionizing the evaluation of patients with CP. In fact, these movement analysis laboratories have given therapists the possibility to obtain precise evaluations before and after surgery and thus to alter their decision making (Bell et al., 2002; Cook et al., 2003). Indeed, CGA permitted to decrease the number of patients recommended for surgery and to change the level or type of surgery in 40% of the cases (Cook et al., 2003). Gait outcomes were found to positively change in patients who received surgery as recommended by CGA (Wren et al., 2011a). A concrete example in which CGA has proven highly beneficial is the Achilles tendon lengthening surgery that was excessively recommended in absence of objective data in case of true equinus or jump gaits (Molenaers et al., 2006). Post-operative CGA data have indeed highlighted the high prevalence of overcorrection evolving

into severe crouch gait, and in certain cases, the loss of walking ability (Pilloni et al., 2019). The number of Achilles tendon lengthening therefore significantly decreased thank to CGA (Molenaers et al., 2006). Grouping multiple single surgical procedures into one single event multilevel surgery was also among CGA's contributions, reducing significantly the frequency of orthopedic surgical procedures (Molenaers et al., 2006). CGA also contributed to increasing the age of the first surgical procedure (Molenaers et al., 2006).

2.3.6.2 « Everyone is speaking a different language »

Unlike the previously mentioned 'Pro' statements, some researchers have painted a gloomy picture of the situation, putting in doubt the evidence supporting the clinical efficacy of CGA in children with CP. Wright J.G., an orthopeadic surgeon, wrote 2 editorials a decade apart (2003 and 2015) in this direction, alarming that « everyone is speaking a different language » (Wright and Theologis, 2015). Given the limitations presented in the previous section (2.3.5 Limitations), reliability and validity of gait analysis seem insufficient. Key multicenter studies (Noonan et al., 2003; Skaggs et al., 2000) indeed raised the concerns and generated a debate (Davids, 2006; Gage, 2003; Wright, 2003) while they demonstrated that substantial differences were found in the raw data acquired on the same patient with CP in different gait analysis institutions and that the treatment recommendations diverged in most cases (Noonan et al., 2003; Skaggs et al., 2000). This variability among examinations arises from the material and technician's performances, the patients' intrinsic variability, and the clinicians' understanding and reasoning (Wright, 2003). Nevertheless, it is worth mentioning that the same variability issue can be found in therapeutic recommendations from other medical examinations. For instance, using the same X-ray images, different treatment decisions can be made by several clinicians for the treatment of scoliosis (Vitale et al., 2011). This evidence supporting clinical low efficacy of CGA in CP emphasized the need to standardize the examination allowing everyone to speak the same language.

2.4 Conclusions

Despite all the limitations and the controversy, CGA is considered as the clinical standard for the quantitative characterization of gait. The fields of investigation are multiple (kinematics, kinetics, muscular activity, plantar pressures, etc.) which require various equipment and a multidisciplinary team. CGA allows the caregivers identifying the gait alterations and their possible causes that will be used to develop a therapeutic plan. This clinical evaluation has proven its clinical relevance for 20 years now and continues to progress to overcome the remaining drawbacks. Engineers and clinicians, whose collaboration has contributed to this success, do not lack inspiration and motivation to generate solutions for better medical care of patients with gait disorders.
The good knowledge of CGA procedure has driven the choices along this doctoral work, i.e. efforts were indeed made to give an overview of the children's gait through multiple variables that are used in CGA and well understood by the clinicians. Hence, the focus of this project was to keep as close as possible from current clinical habits, in order to end up with reasonable and realistic propositions.

Chapter 3 *

Real-life measurement: Spatiotemporal gait parameters assessment using wearable technology – State of the art

Abstract

Methods for the estimation of spatiotemporal parameters of gait using wearable devices have emerged for nearly 30 years now. Several computational approaches have been developed, using different configurations of sensors. This chapter aims at reporting a global overview of the mostly used systems, in a technical review format. Published articles were exported from five relevant databases. Full-length articles published in English, including studies using wearable systems to estimate one or several spatiotemporal parameters in pathological or non-pathological populations were considered. Included articles were classified into two groups depending on if the article described a new method or used an existing method. Articles describing a new method were discussed regarding the sensor configurations, the computational approaches, the performance of the system, in three distinct sections namely, temporal, spatial and spatiotemporal parameters. This chapter ends with a section dedicated to the use of such methods in the particular case of children with cerebral palsy.

* Part of this chapter intended for a future publication with the following co-authors:
Carcreff L., Scott K., Soltani A., Bonci T., Kuederle A., Mico E., Ullrich M., Cereatti A., Del Din S., Eskofier B., Mazza C., Ionescu A., Aminian K.
My contributions: Conceptualization, methodology, paper selection, part of screening, data extraction, writing – original draft preparation

3.1 Introduction

Quantification of gait parameters is highly prized for clinicians caring patients with gait disorders. Traditionally, the gold standards for gait parameters computation are specific cutting-edge equipment (described in Chapter 2) which have limited accessibility due to their high cost, the need of a dedicated room (gait analysis laboratory), the need of qualified and dedicated personnel, and the time required for patient preparation, data acquisition, processing, and interpretation (Petraglia et al., 2019). Furthermore, limited space entails that patients are evaluated along short walking distances, and only a few steps are assumed to be a good reflection of their usual gait (Aminian et al., 2002). To overcome these limitations, researchers have begun to take advantage of accelerometer allowing ambulatory monitoring since the 1970s. Later with the progress of Micro-Electro-Mechanical Systems (MEMS) the use of such sensors has increased with the combination of accelerometer and gyroscope and according to the rapid development of microcontroller power, memory card capacity, and battery size and autonomy (Kumar Mishra et al., 2019).

Inertial sensors, magnetometers and force and pressure sensors are the most used wearable sensors nowadays (Tao et al., 2012). 'Inertial' refers to the ability of sensors to measure their movement, or the movement of a rigid body to which it is attached, exploiting the reluctance of an internal free mass to move (inertia) while being accelerated or rotated by an external force (Picerno, 2017). Inertial sensors also called 'Inertial Measurement Units' (IMU), include accelerometers, sensing linear acceleration along a sensitive axis, and gyroscopes, sensing angular velocity about a sensitive axis (Picerno, 2017). Nowadays, most IMUs comprise 3D accelerometer and 3D gyroscope with 3 orthogonal sensitive axes. The extended appellation 'Magneto-Inertial Measurement Units' (MIMU) encompasses a magnetometer, measuring the earth's magnetic field orientation, in addition to the IMU components (Petraglia et al., 2019). Pressure sensors and force-sensitive resistors (FSR), measuring pressure and force respectively, have the potential to quantify plantar pressures and the distributed vertical component of the ground reaction force (Hegde et al., 2016). Finally, barometric pressure sensors can be used to estimate the sensor elevation (Moufawad el Achkar et al., 2016).

These sensors properties allow computing gait parameters such as spatiotemporal parameters (STP), kinematics and kinetics. Methods to estimate gait parameters from inertial sensor data have been developed since 1990 (Fong and Chan, 2010; Picerno, 2017; Yang and Li, 2012a). In fact, abundant studies providing methods for ambulant gait analysis have ensued. Systems providing 3D gait kinematics and kinetics developed massively and were found accurate and reliable with regard to the optoelectronic system when used in clinical and standardized settings for healthy subjects (Hegde et al., 2016; Petraglia et al., 2019). Appropriate and precise movements of calibration are often required, implying, at least, the supervision of an investigator each time the sensors are mounted. In addition, 3D kinematic parameters may rely on the use of a magnetometer which has the inherent risk to sense a locally disturbed magnetic field (Picerno, 2017). This means that such system may suffer from inaccuracies in unsupervised real-life settings upon regular contact with ferromagnetic disturbances. On the other hand, STP computation can rely on sensor orientations in 1D, simplifying the calibration procedures (Picerno, 2017). Temporal analysis using the cyclical property of gait can be done by detecting periodic features on acceleration and angular velocity signals (Yang and Li, 2012a). Spatial parameters and STP are explored through numerical integration, biomechanical models or abstraction models (Yang and Li, 2012a). So far, STP might be more exploitable in real-life settings than kinematics or kinetics with wearable sensors due to the possibility to consider 1D signals.

Gait speed and step length reduction, stance time and cadence augmentation are common features related to a decrease in activity level and participation. STP constitute indeed good predictors of disability (Petraglia et al.,

2019). Precise and reliable measures of these fundamental gait parameters are thus of major clinical interest, i.e. for therapy planning and management (Washabaugh et al., 2017). The gold standard systems for the measurement of STP, described in Chapter 2, as well as low-cost instruments such as Kinect or a single RGB camera (Yagi et al., 2019), have the inconvenience of providing only restricted capture volume. Wearable systems have the great advantage to enable the measurement of almost an unlimited number of steps in various environments (Washabaugh et al., 2017). Currently, among all the published methods, variable levels of accuracy are reported depending on the methodological approach and the sensor location (Pacini Panebianco et al., 2018; Petraglia et al., 2019). The purpose of this chapter is to review existing approaches for STP assessment using wearable systems, mostly IMUs, regarding computational methods, sensor configurations, accuracy against a reference, studied population and assessment settings, in order to report the current general trends.

3.2 Method

3.2.1 Articles identification

Although the whole present technical review was not meant to be systematic, the most relevant clinical and technical databases were consulted using specific keywords. Articles were selected from PubMed (Medline), Embase, Web of Science, Scopus and IEEE Xplore databases in February 2019. Full-length articles published in English, including studies using wearable systems to estimate one or several gait STP in humans (with or without pathology) were considered. The logical search equation was: ((walking OR gait) AND ("inertial sensor" OR "kinematic sensor" OR "miniaturized sensor" OR "body fixed sensor" OR "body worn sensor" OR "inertial device" OR "wearable device" OR "kinematic device" OR "body fixed device" OR "body worn device" OR "inertial system" OR "wearable system" OR "inertial measurement unit" OR "imu" OR “mimus” OR “imus” OR "miniaturized inertial measurement unit" OR "mimu" OR "GPS" OR " global navigation satellite system" OR accelerometer OR gyroscope OR "angular rate" OR "angular velocity" OR "mobile phone" OR "cell phone" OR smartphone) AND (“speed” OR “gait velocity” OR “walking velocity” OR “cadence” OR “spatiotemporal” OR “spatio-temporal” OR “gait parameter” OR “gait parameters”) AND (algorithm OR assessment OR measurement OR technique) AND NOT ("Animal" OR "Animals")). The search was based on the title, abstract and keywords.

3.2.2 Studies selection

After duplicates removal, using the Mendeley reference management software (*https://www.mendeley.com*), and exclusion of records based on keywords, the titles, and abstracts of the remaining records were read to exclude irrelevant results according to the following exclusion criteria. Articles were excluded if (1) they were not an original article (i.e. case reports, reviews, conference proceedings commentaries, letters to the editor or theses), (2) they were not related to the assessment of human gait, (3) only one subject was assessed (poor level of evidence), (4) the monitoring system used was not wearable or non-independent from a non-wearable device, (5) the monitoring system was not usable indoor or outdoor, (6) none of the following STP was computed: number of steps, cadence, stride time, stride length, stride velocity and gait phases duration, (7) the computational method was not described or referenced, (8) any validation measure was reported (if the computational method was described), and (9) the article was not written or translated in English. Included records were separated in 2 groups depending if the article was describing a new method or using an existing method. For this chapter, and for the purpose of the intended publication, we only focused on the first group to have a technical overview of the methods. However, at the end of this chapter, a section is dedicated to the use of these methods in the particular case of children with CP.

3.2.3 Data extraction

Included full-text articles were screened to extract information regarding computational approaches, sensor configurations, validation of the system for the estimated temporal, spatial, spatiotemporal parameters and experimental procedures.

3.3 Results and discussion

Figure 20 details the process for articles inclusion.

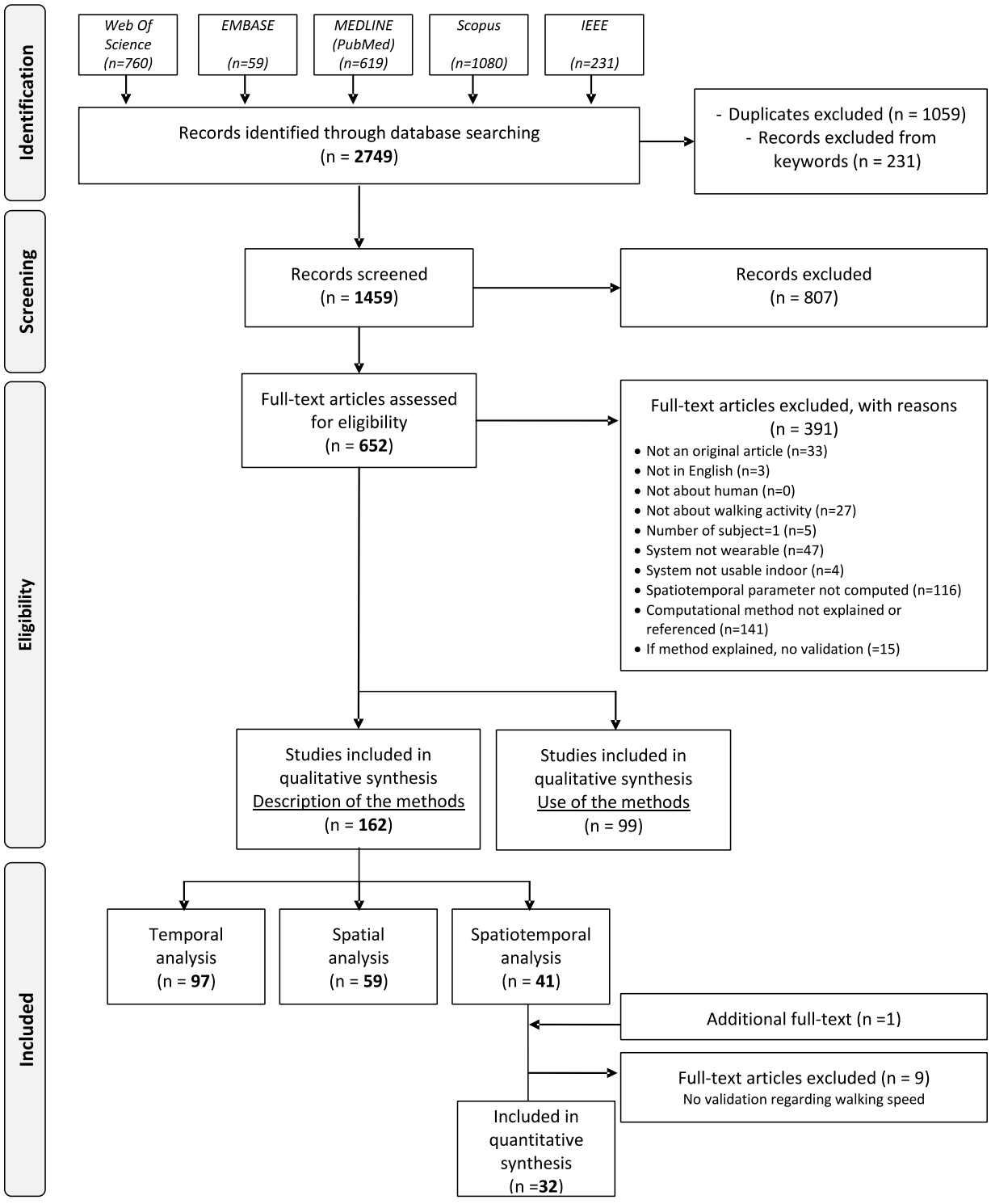


Figure 20 - Flow diagram of the literature review concerning the assessment of spatiotemporal gait parameters with wearable devices

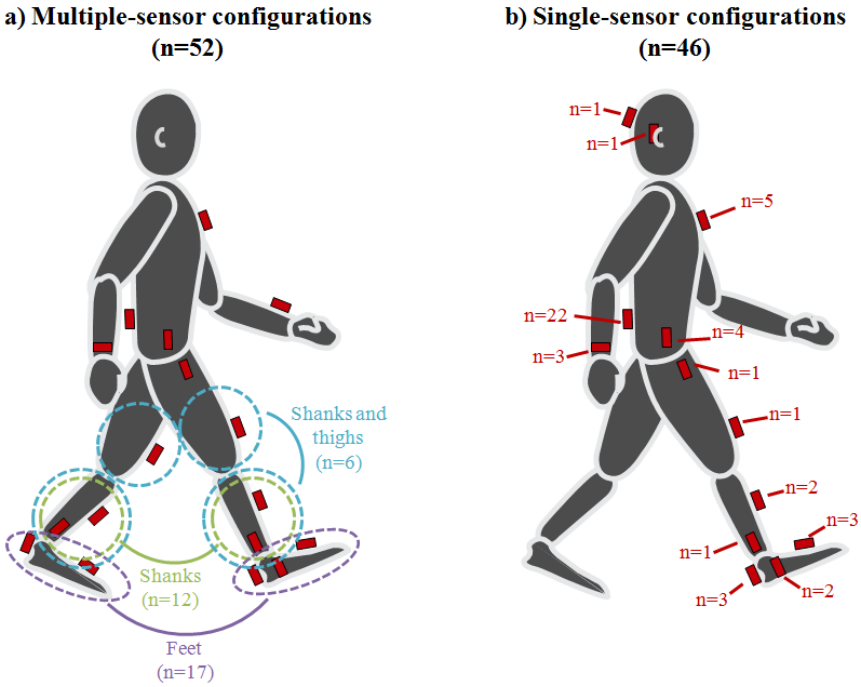
From a total of 2'749 articles identified through the database search, 162 were included as a description of a new method, and 99 were included as an evaluation of an existing method. Among the studies describing a new method, 97 were dedicated to estimating temporal parameters, 59 estimated spatial parameters and 41 estimated walking speed. The latter category of results was the primary focus of the intended publication (cf first page of the Chapter, page 39) so a more exhaustive data extraction was carried out. Nine articles within this subselection did not provide any validation metrics regarding walking speed since it was computed as the ratio between the time and the estimated traveled distance. These 9 papers were excluded for further analysis. Result articles were published between 1992 and February 2019.

3.3.1 Temporal parameters

Ninety-seven studies were reviewed for the estimation of temporal parameters which include gait events foot strike (FS), foot off (FO)), number of steps, cadence, stride time and gait phases duration. Gait events detection is mostly discussed since stride time and gait phases duration depends on the accuracy of gait events timing.

3.3.1.1 Sensor configurations

Figure 21 illustrates the main sensor configurations found for temporal gait parameters estimation.



In (a) only the number of studies of the most reported multiple-sensor configurations (Feet, Shanks and Shanks and Thighs) are represented for clarity reasons.

Figure 21 – Existing sensor locations used in multiple (a) or single (b) configurations for temporal gait analysis with the number of studies found for the corresponding sensor location

Most of the studies used a sensor located on the lower back, generally at the 4th or 5th lumbar vertebrae level (L4-L5), close to the subject's center of mass (COM) to detect temporal features of gait. This location is very convenient since it can be worn on a belt. The two other commonly used configurations are the shanks-configuration and the feet-configuration which necessitate two sensors. The placement of the sensors on the feet varies a lot across the studies (on the top of the shoes (Lee et al., 2018; Mariani et al., 2013a; Patterson and Caulfield, 2011), on the medial side (Anwary et al., 2018a) or at the heel level (Misu et al., 2014; Razak et al., 2018; Rebula et al., 2013). Other, less common, configurations include upper trunk (sternum pendant)

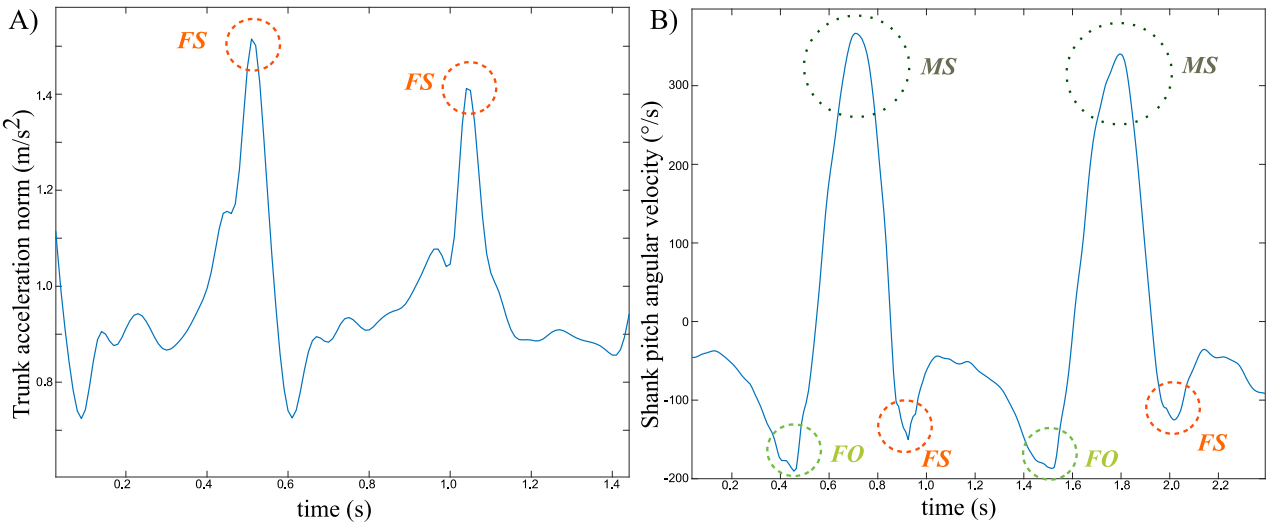
(Brodie et al., 2015), wrist (Cho et al., 2016; B Fasel et al., 2017), head (Hwang et al., 2018), ear (Jarchi et al., 2014), thigh (Aminian et al., 1999; Miyazaki, 1997) or trousers pocket close to the hip (Avvenuti et al., 2018; Muñoz-Organero et al., 2017).

3.3.1.2 Computational approach

Four main families of approach can be found to compute temporal features of gait: event detection, frequency analysis, template matching, and machine learning. From the time events extracted, all temporal parameters of gait can be deduced.

Event detection

The overwhelming majority of systems computing temporal features of gait from inertial sensors, i.e. accelerometer or gyroscope signal, uses a method of peak detection. Signal characteristics belonging to a specific temporal event of the gait cycle (mainly FS and FO) are indeed recognized through local maxima or minima, or using particular thresholds. During gait, anteroposterior acceleration, vertical acceleration or the norm of acceleration are particularly high at initial and terminal contacts (Sejdic et al., 2016), so local peaks can be easily identified (Figure 22A) by sensors located on the lower back (Cho et al., 2016; Kikkert et al., 2017; Kosse et al., 2015; Sejdic et al., 2016), the heels (Lee et al., 2018; Razak et al., 2018), the head (Hwang et al., 2018), etc. The systems using sensors on the shanks or the feet exploit particularities of the angular velocity signal. Indeed, the swing phase of a gait cycle is characterized by a positive shank angular velocity reaching its highest values at around midswing (MS). This method was first described by Aminian et al. (Aminian et al., 2002) and used by several studies (Ferrari et al., 2016; Mariani et al., 2010; Misu et al., 2017; Salarian et al., 2004). The local minima before and after MS are thus considered as FO and FS respectively, as illustrated in Figure 22B.



Abbreviations: 'MS': midswing; 'FS': foot strike; 'FO': foot off

Figure 22 - Peaks on trunk acceleration norm (A) and shank pitch angular velocity (B) signals corresponding to midswing, foot off and foot strike areas

Based on these principles, several studies proposed improved methods for event detection. For the methods using gyroscope data, Botzel et al. demonstrated that FO was more accurately detected somewhere between the first trough of angular velocity and the zero-crossing time rather than between the trough and the MS peak (Bötzel et al., 2016). Mariani et al. demonstrated that the best features to detect FS and FO with sensors on the

feet were the local minimum and maximum peaks of the norm of acceleration respectively, as compared to zero crossing, threshold surpassing or using gyroscope data (Mariani et al., 2013b). Instead of using raw inertial signals, some methods use computed angles or other processed signals to detect temporal features (Bussmann et al., 2004).

During a gait cycle, the foot is supposed to be flat and static during midstance. Zero acceleration or velocity can thus help to determine temporal events of gait with sensors on the feet (Fourati, 2015; Mariani et al., 2010; Qiu et al., 2016; Rebula et al., 2013). Similarly, shank angular velocity during midstance neighbors zero and can also be used for stride segmentation (Li et al., 2010; Yang et al., 2013). This approach has, however, the drawback to be inappropriate for some pathological gaits like those of toe walkers or patients with crouch gait.

Frequency analysis

Since gait is a cyclical activity, frequency analysis is also commonly used to determine the cadence. Fast Fourier Transform (FFT) is thus performed on one axis or the norm of acceleration (Demonceau et al., 2015). The fundamental frequency is chosen and refers to the stride or the step frequency depending on if the sensor is located on body extremities (upper or lower limbs), e.g. the wrist (B Fasel et al., 2017), or the central part of the body (i.e. trunk and head) (Nagai et al., 2014; A Paraschiv-Ionescu et al., 2019; Punt et al., 2014) respectively.

FS and FO events can be well identified in the time domain but also in the frequency domain thus wavelet transformation is adapted for their identification, followed by a peak detection method. Indeed, wavelet processing allows enhancing FS and FO through iterative decompositions and this eases the peak detection. This approach has been proposed in several studies (Aminian et al., 2002; Hickey et al., 2017a; Majumder et al., 2019).

Template matching

A minority of studies proposed a template matching method based on the detection of all periodic intervals from a signal resembling in shape and magnitude to a predefined template (Micó-Amigo et al., 2016; Muñoz-Organero et al., 2017). This approach seems to be valid for short duration monitoring (Micó-Amigo et al., 2016).

Machine learning

Last but not least, machine learning approaches are exploited for step detection as well as gait events identifications. Hidden Markov-based method (Mannini et al., 2014), signal vector magnitude (Hsu et al., 2014), Bayesian inference (Martinez-Hernandez and Dehghani-Sanij, 2018) or fuzzy inference (Senanayake and Senanayake, 2010) systems have been developed for specific populations and applications. Inputs of these models are mostly acceleration and/or angular velocity features, such as the variance of the signal vector magnitude of acceleration or angular velocity (Hsu et al., 2014), the vector of stride-normalized angular velocity (Mannini et al., 2014), or the fundamental frequency of accelerations (Yuwono et al., 2014), but joint angles and FSR inputs were also used (Senanayake and Senanayake, 2010). Indeed, the inconvenient of these approaches is the generalization since a subset of data is used to train the models. Furthermore, a large amount of training data is needed which is sometimes difficult to find, especially in pathological populations.

With sensors other than MIMU

A few records reviewed used other types of sensors. FSR and some pressure sensors have the possibility to be freely worn under the feet, hence they have been used for temporal events detection during gait over long distance. These sensors were often reported as reference systems to validate IMU systems in real-life

environments (Aminian et al., 1999; Avvenuti et al., 2018; Chang et al., 2016; Figueiredo et al., 2018; Han et al., 2019; Lee and Park, 2011; Misu et al., 2017; Sabatini et al., 2005). The approach with those sensors is to detect when the signal (force or pressure) passes a certain threshold corresponding to the instant of FS and when the signal passes below the same or another threshold corresponding to the foot leaving the ground (TO) (Arafsha et al., 2018; Djurić-Jovičić et al., 2014). Infrared time-of-flight distance sensors can be used as well to count the number of steps. When placed on the medial side of the feet, these sensors return a distance indication when the feet face each other, i.e. at each step. Step detection is thus possible by directly counting the non-zero distance values (Bertuletti et al., 2019). This system has the advantage of providing additional gait parameters such as step length and stride width as mentioned in section 3.3.5. meaning that it can constitute a valid alternative to IMUs for real-life measurements. Microphone sensors were also reported in a study (Wang et al., 2016) collecting footstep sounds during walking. The temporal parameters were thus estimated from acoustic signals.

Nevertheless, all these sensors have the drawback to be dependent on shoe-wearing leading to the potential missing of a large part of home-based locomotion activities.

3.3.1.3 Performance of the systems

Accuracy of the systems is mostly evaluated against FSR, optoelectronic system, force plates or pressure mat (such as GaitRite, CIR Systems Inc., PA, USA) in laboratory settings. Reported results of accuracy (relative/absolute mean error, root mean square error, correlation coefficient, t-test p-value, etc.) vary a lot across the studies, hence it is very difficult to compare the performances of the methods based only on the publications. Among the articles that reported relative errors for FS and FO detections, between 5 and 20ms error was found mostly in healthy participants (Bejarano et al., 2015; Greene et al., 2010; Hanlon and Anderson, 2009; Hundza et al., 2013; Lee et al., 2010; Sejdic et al., 2016). This is in line with a recent review of Pacini Panebianco et al. who tested 17 existing algorithms on a single data set of 35 healthy adults walking with 5 IMUs (Pacini Panebianco et al., 2018). They concluded, in agreement with other authors (Iosa et al., 2016; Washabaugh et al., 2017), that the closer the sensor is to the ground the better performances will be found for gait event detection. The peak detection method was found the most accurate, independently from the sensor location. Finally, they found that there was no influence of the sensor configuration for FS detection and that the feet-configuration conferred higher accuracy for FO detection (Pacini Panebianco et al., 2018). Overall, IMU-based gait event detection demonstrated a delay for FS and anticipation for FO, which had thus no consequence on stride time computation (<0.1s) but quite large consequences on stance time estimation (up to 0.2s) (Pacini Panebianco et al., 2018).

Several studies proposed to validate their system in semi-controlled settings, such as during a sequence of daily-life-like activities (e.g. inclined walking, indoor, outdoor, staircase …). Figueiredo et al. for instance used FSR as a reference for gait event detection in such simulated real-life situations with healthy adults (Figueiredo et al., 2018). Good accuracy was reported for every gait event computed in such conditions with their system (>90% among all conditions and events). Very few studies reported the validation of temporal parameter estimation in real-life settings. Hickey et al. put a GoPro camera (GoPro Inc, CA, USA) attached to the participant's chest as a reference system for step detection during almost 20h of unscripted free-living activities (Hickey et al., 2017). Excellent relative agreement and no bias were found between their wearable system and the camera (Hickey et al., 2017). Derungs et al. used a manual stride annotation completed by an external observer in a day-care therapy center as a reference for stride duration, cadence and stride count in hemiplegic patients during 9.3 days on average, 8h per day (Derungs et al., 2018). Average relative errors were reported below 6% between this manual annotation and the wearable system (sensors on wrist, arms, and thighs).

3.3.2 Spatial parameters

Fifty-nine studies were reviewed for the estimation of spatial parameters which include stride and step length.

3.3.2.1 Sensor configuration

For spatial parameter computation, the majority of studies reported sensors located on the feet or shoes (10 in multiple-sensor configurations and 11 for single-sensor configurations). Waist-configurations, shanks-configurations, and shanks-and-thighs-configurations were also largely used (Figure 23). Besides, several single-sensor configurations were found such as a sensor on the head (Hwang et al., 2018), a smartphone in the hand (Liu et al., 2015), a sensor around the hip (Sharp and Yu, 2014), the thigh (Miyazaki, 1997) or the shank (Yang and Li, 2012b).

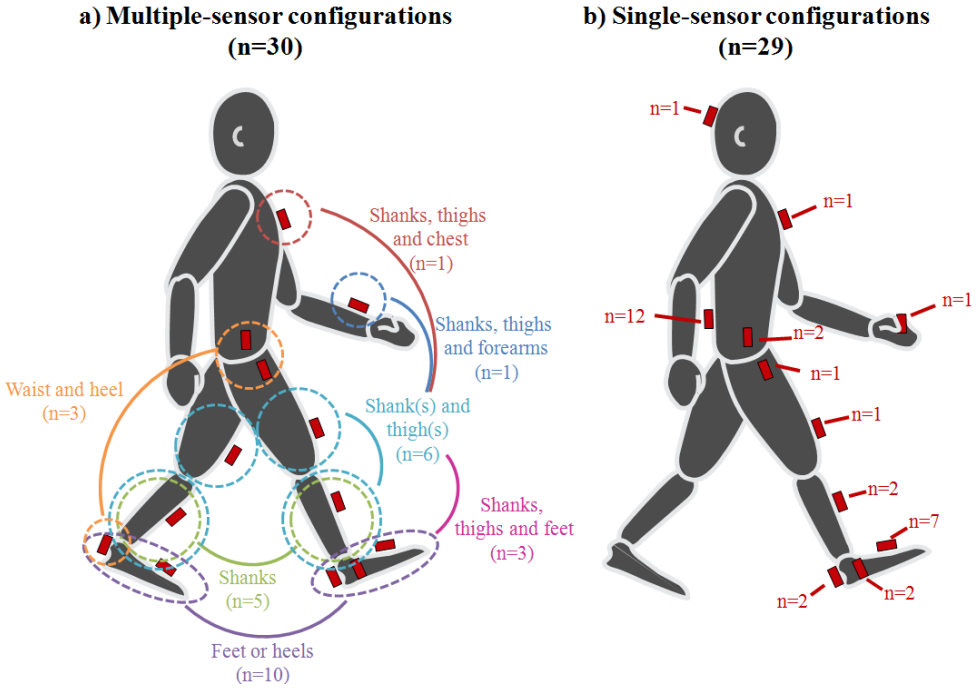


Figure 23 - Existing sensor locations used in multiple (a) or single (b) configurations for spatial analysis with the number of studies found for the corresponding sensor location

3.3.2.2 Computational approach

Two categories of spatial parameter estimation approaches exist: direct computation through the integration of acceleration and indirect methods relying on models, which can be biomechanical models or statistical models.

Integration

First, the most common computational approach to estimate the stride length is the numerical integration of accelerometer data. Indeed, double integration of the acceleration in the forward direction results in positions, so stride length can be directly computed as the sensor position difference between two identical events of successive gait cycles (FS by convention, or other events like foot-flats (Mariani et al., 2010) for example). In most studies, the 3D IMU orientation is first estimated using accelerometer, gyroscope and possibly magnetometer data. The initial orientation is indeed estimated from the 3D accelerations. Then the IMU orientation is computed with the strap-down integration, i.e. 3D integration of the angular velocity. The gravity component is removed from the accelerations expressed in the global frame. These steps permit to select the forward linear acceleration which is further integrated by trapezoidal integration to obtain linear velocity. And

finally, the de-drifted velocity (cf following paragraph) is integrated to estimate the position. Figure 24 is an illustration of this common process proposed by Rebula et al. (2013). Sensor orientation can also be estimated through a Kalman filter which fuses the inclination from accelerometer data and orientation obtained from the integration of angular velocity by adapting the weights given to the signals depending on the amount of acceleration (Fasel, 2017; Luinge and Veltink, 2005; Mazzà et al., 2012). This computation allows reducing the drift effect (Fasel, 2017; Rebula et al., 2013).

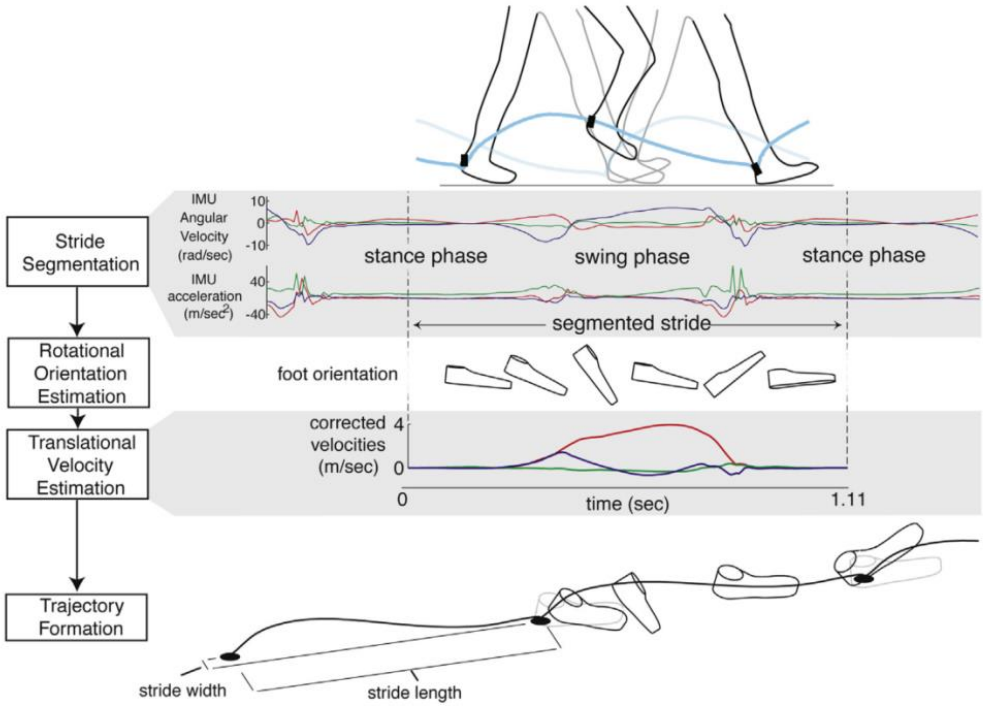


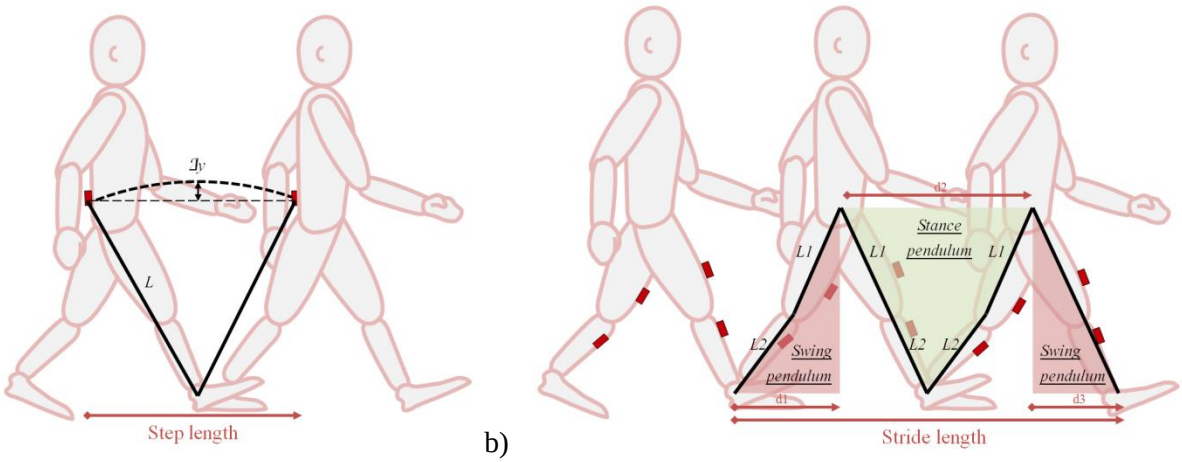
Figure 24 – Common process to estimate the stride length through the integration method with sensors on the feet (Rebula et al., 2013)

Inertial sensors inherently comprise noise and time-varying offset which leads to an accumulating drift when the signal is integrated over a long period of time (Djurić-Jovičić et al., 2012). This constitutes the major issue with the integration approach. Many methods were developed to avoid this effect of drift, setting initial and terminal conditions for integration per strides. These methods include zero velocity update (ZUPT) (Anwary et al., 2018a; Cho et al., 2018; Mannini and Sabatini, 2014; Mariani et al., 2010; Qiu et al., 2016; Rampp et al., 2015; Rebula et al., 2013; Sabatini et al., 2005; Song and Kim, 2018) or updates using other significant periodic event proper to the population and the biomechanical properties of the movement (Jarchi et al., 2018). ZUPT is used especially when sensors are located on the feet since the feet are supposed to be flat on the ground at each midstance for able-bodied subjects. However for the other sensor configurations like waist-configuration (Bugané et al., 2012; Schutz et al., 2002; Shieh and Cho, 2013), shank-configuration (Li et al., 2010), wrist-configuration (Duong and Suh, 2017) or head-configuration (Hwang et al., 2018) ZUPT was also used but it is more difficult to set (Diez et al., 2018). With a shank-configuration, for instance, the instant when the shank angle is equal to zero (aligned with the vertical) is used to set the initial conditions for integration (Li et al., 2010; Yang and Li, 2012b).

In a minority of studies (5%), the forward linear acceleration was obtained from a uniaxial accelerometer or assumed to be one of the axes pointing the direction of travel. This 1D acceleration is thus double-integrated at each stride interval to estimate the stride length (Bugané et al., 2012).

Biomechanical models

Due to the mechanical property of human gait, geometrical relations between the length and orientations of body segments and the stride length can be established. Various biomechanical models, making different simplifications or assumptions, have thus been developed (Diez et al., 2018). Two main types of models are currently used: the single pendulum models, mainly called "inverted pendulum", and the double pendulum models. The former assumes that the COM rotates as an inverted pendulum with a length equals to the leg length about the ankle during the single stance phase, followed by horizontal displacement during the double support phase. The displacement during the double support phase can be approximated in different ways, for example by a constant or by another vertical displacement of the COM (Zijlstra and Hof, 2003). The step length can thus be estimated only from the vertical displacement of the COM and the leg length (Figure 25a). Several models with various levels of complexity and various calibration parameters have been developed (Diez et al., 2018). COM displacement is commonly measured from an accelerometer located at lumbar region such as L4-L5 level (Zijlstra and Hof, 2003). Shanks and thighs angular velocities were later exploited by some authors to indirectly estimate the COM displacement (Aich and Kim, 2018; Allseits et al., 2018). The double pendulum model initially proposed by Aminian et al. is based on two pendulums with the length of the shank and thigh rotating around the hip and knee during the swing phase and an inverted double pendulum rotating around the ankle and knee during the stance phase. Shank and thigh rotation in sagittal plane are computed during stance and swing phases from gyroscope sensors to estimate the stride length (Figure 25b) (Aminian et al., 2002). For these biomechanical model approaches, numerical integration of acceleration or angular velocity is also required. However, the integration is usually performed in sagittal plane over short time intervals for the drift effect to be negligible.



a) b)

L: leg length
Δy: vertical COM displacement estimated by double integration of vertical acceleration

L1: thigh length
L2: shank length
d1 and d3: estimated distances in the swing pendulum
d2: estimated distance in the stance pendulum

Figure 25 - Biomechanical models for step or stride length estimation: the inverted pendulum (a) (Zijlstra and Hof, 1997), and the double pendulum (b) (Aminian et al., 2002)

Statistical models and machine learning techniques

The simplest statistical model is the linear regression between step or stride length and step or stride frequency, from what leg length, height or a tunable constant can be added (De Silva et al., 2018). More recently, regression models estimated stride length exploiting its relationship with the root mean square (RMS) of the raw acceleration for instance (Punt et al., 2014). Machine learning techniques are more and more used to

estimate stride length from a variety of different gait features like time (e.g. stride time, gait phases duration), frequency (e.g. cadence) or amplitude features (e.g. median, minimum, maximum, standard deviation of the amplitude of the signal or at specific instants of the gait cycle, covariance between two signals) collected from accelerometers, gyroscopes and/or constants such as anthropometric data (Aminian et al., 1995a; Liu et al., 2015; Mannini and Sabatini, 2014). Neural network (Aminian et al., 1995b, 1995a; Hannink et al., 2017; Liu et al., 2015) is the most reported method.

3.3.2.3 Performance of the systems

Authors reported using fixed distances or fixed step lengths over ground or on a treadmill as reference to validate their systems (about 45% of the screened articles). The other most reported reference systems for spatial parameter estimation were the optoelectronic system (33%) and instrumented mat (11%). Similar to articles including temporal parameters, the type of validation metrics are very heterogeneous to draw direct conclusions about the best systems. Vezocnik et al. (2019) have evaluated the performance of 13 representative average step length estimation methods on healthy subjects with a Smartphone at different locations. They have determined that regardless of the computational approach and the sensor location, the error was found between 5 and 10% of the step length, being in average between 3.6 and 7.2cm, for wide ranges of speed (from 0.5 to 2.0m/s). Regarding biomechanical models, the performances can depend on the complexity of the model, i.e. the inclusion of pelvic rotation (Hu et al., 2013) or feet length (González et al., 2007).
The large majority of studies reported validation under controlled settings, in a laboratory. However, similar to the section on temporal parameters, semi-standardized routes were also employed. In these case, the reference was a fixed distance to travel, e.g. along the hospital corridors, in a hallway, on the street or on an athletic field (Djurić-Jovičić et al., 2014; Liu et al., 2015; Yun et al., 2012; Zhao et al., 2019). No study reported actual real-life settings.

3.3.3 Spatiotemporal parameter

Thirty-one studies were found to give validation measures about walking speed. An additional study (Soltani et al., 2019), which was published after February 2019, was added to the selection since it met all the inclusion criteria and was relevant to the review. This section about walking speed estimation constituted the main focus of the intended publication. Figure 26 summarizes the configurations, the computational methods, the sensor modalities and the reference systems used for the validation of the methods included. The performances of the systems are indicated when they were reported as a percentage of the walking speed. Three studies (Mannini and Sabatini, 2014; McGinnis et al., 2017; Schimpl et al., 2011) developed several methods or used several sensor configurations, and compared them in their publication, so all of their methods were considered separately in Figure 27.

3.3.3.1 Sensor configurations

The repartition between single and multiple sensor configurations was found to be about 50-50%. Regarding multiple sensor configurations, the shanks configuration was the most used (Aich et al., 2018; Dobkin et al., 2011; Doheny et al., 2010; Li et al., 2010; Salarian et al., 2013; Yang et al., 2013), followed by the shank(s)-and-thigh(s) configurations (Allseits et al., 2018; Aminian et al., 2002; McGinnis et al., 2017; Motoi et al., 2012; Salarian et al., 2004). Regarding single sensor configurations, the waist configuration was by far the most reported (Bonomi and Salati, 2010; Bugané et al., 2012; Hu et al., 2013; McGinnis et al., 2017; Perrin et al., 2000; Schimpl et al., 2011; Supratak et al., 2018; Zijlstra and Hof, 2003). The foot configuration was also often reported (Brzostowski, 2018; Mannini and Sabatini, 2014; Sabatini et al., 2005; Song and Kim, 2018).

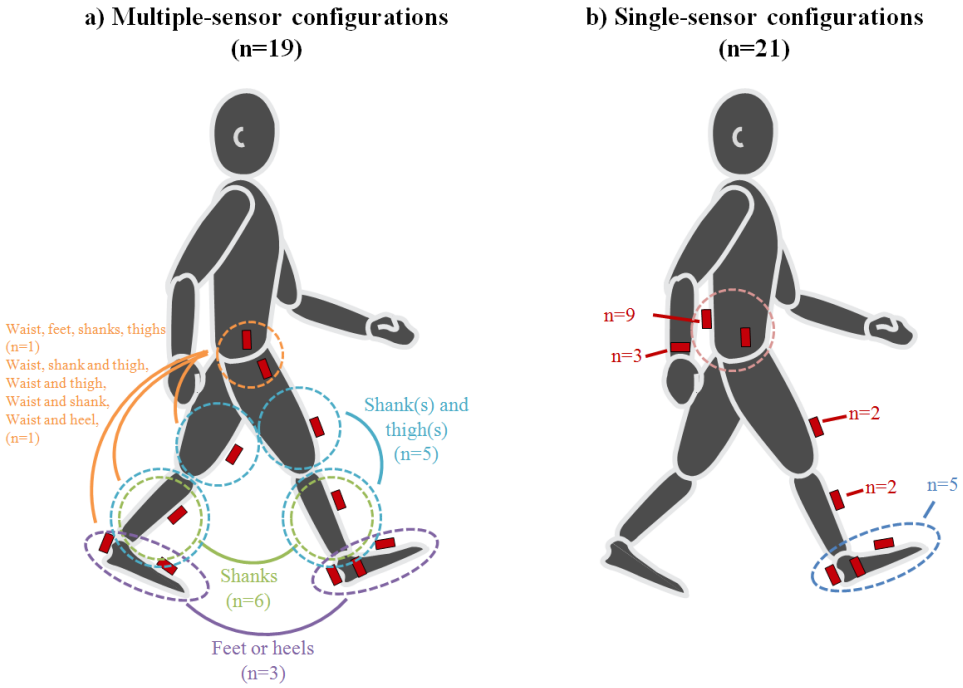


Figure 26 - Existing sensor locations used in multiple (a) or single (b) configurations for spatiotemporal analysis with the number of studies found for the corresponding sensor location

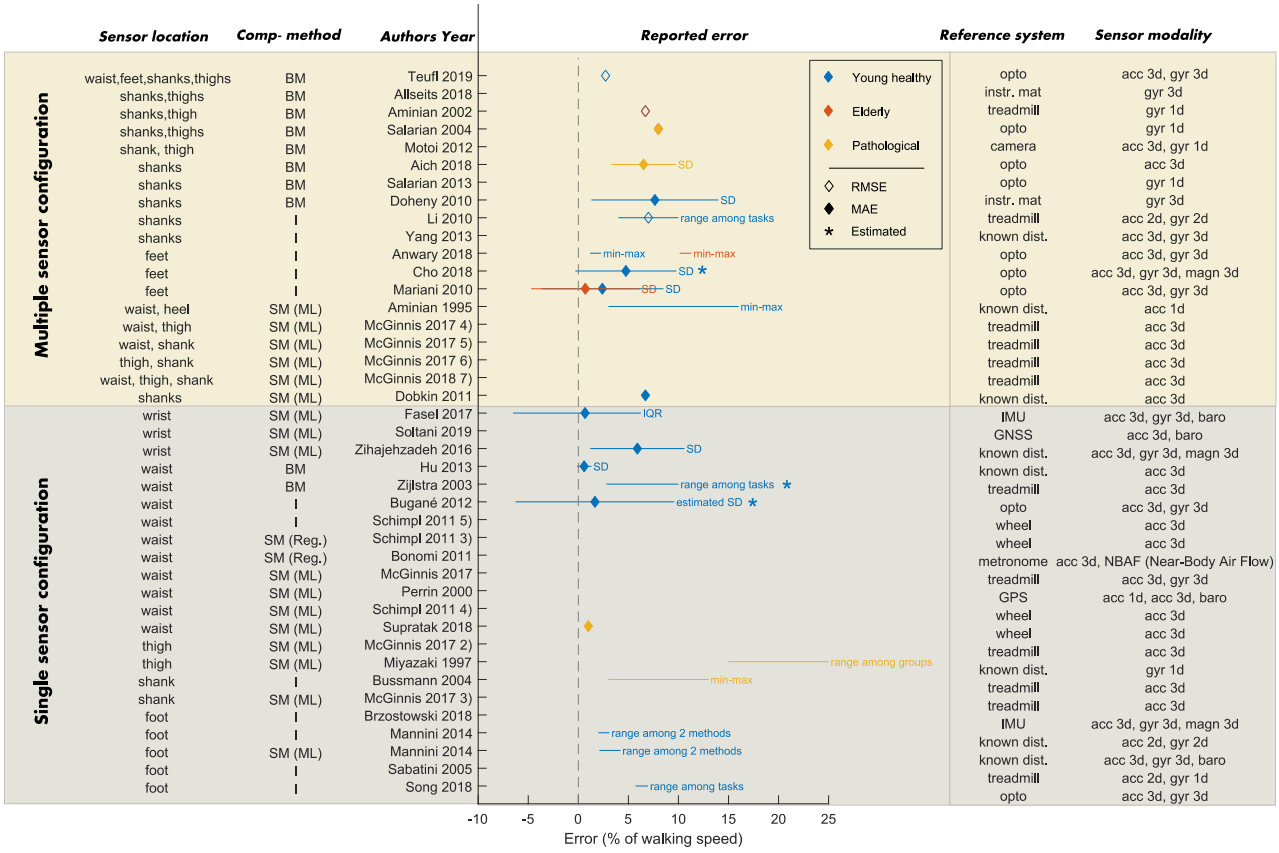
3.3.3.2 Computational approach

Walking speed can be estimated from the ratio between stride length and stride time, using the previously described methods (sections 3.3.1 and 3.3.2). Besides, similarly to spatial parameter estimation, direct integration or machine learning approaches can be used. Twelve studies were found to use the direct integration method. In this case, the linear horizontal acceleration of the body segment is integrated once to obtain the velocity. Similarly to double integration for stride length estimation, initial and terminal conditions need to be set and differ between the methods and configurations (ZUPT or others). Ten studies used a biomechanical model to compute the stride length and then the walking speed. The others used statistical approaches, i.e. regression or machine learning. Twelve studies used machine learning approaches. Between ten (Aminian et al., 1995b) and forty-one (Schimpl et al., 2011) linear, angular and biometric features were defined in the time and frequency domains to train the models. Two studies used also barometric or global navigation satellite system (GNSS) features (B Fasel et al., 2017; Soltani et al., 2019). The most common approach for the validation of the model was the leave-one-subject-out cross-validation (Mannini and Sabatini, 2014). Two studies exploited the regression between the step length and the acceleration norm (Bonomi and Salati, 2010) or the step frequency (Schimpl et al., 2011) to estimate the walking speed.

3.3.3.3 Performance of the systems

The most used reference systems for walking speed estimation validation were the treadmill, the optoelectronic system and known distance and time of travel (Figure 27).

Performances comparison is provided in Figure 27. Only the studies reporting root mean square error (RMSE) or mean absolute error (MAE) in percentage of the speed, or reporting enough information to estimate the error in percentage of the speed, were reported.



Abbreviations: 'Comp. Method': Computational method; 'BM': Biomechanical model; 'I': Integration; 'SM': Statistical model; 'ML': Machine learning; 'Reg.': Regression; 'RMSE': Root mean square error; 'MAE': Mean absolute error; 'Estimated': mean error estimated from values reported in the papers; 'SD': standard deviation; 'IQR': Interquartile range; 'GNSS': Global navigation satellite system; 'opto': optoelectronic system; 'instr. Mat.': instrumented mat; 'known dist.': known distance; 'acc': accelerometer; 'gyr': gyroscope; 'magn': magnetometer; 'baro': barometer. Numbers next to the author names and year refers to different methods within the same publication.

Figure 27 - Data extraction from studies computing and validating walking speed from wearable devices according to sensor location, computational method, first author, year, reported error, reference system and sensor modality

Figure 27 reveals that the errors are mostly contained between 0 and 10% of the walking speed independently from the computational approach, the sensor configuration or the population on which the system was validated. Most of the studies tested their system on a young and healthy population. Five studies validated their system with elderly people (Aminian et al., 2002; Anwary et al., 2018a; Bonomi and Salati, 2010; Mariani et al., 2010; Salarian et al., 2004). Within the pathological populations, patients with Parkinson's Disease (Aich et al., 2018; Salarian et al., 2004), with Multiple Sclerosis (McGinnis et al., 2017; Supratak et al., 2018), with coxarthrosis (Salarian et al., 2013), after stroke (Dobkin et al., 2011; Yang et al., 2013), amputees (Bussmann et al., 2004; Miyazaki, 1997) or hemiplegic patients (Miyazaki, 1997; Motoi et al., 2012) were evaluated. With the exception of the study of Miyazaki et al. (Miyazaki, 1997), the performances of the methods were not highly decreased with pathological populations (until 13% of error).

McGinnis et al. have compared five different sensor configurations with a machine learning approach and found similar results of performances across the five configurations (RMSE < 0.15m/s for healthy subjects and RMSE < 0.16m/s for patients with Multiple Sclerosis) (McGinnis et al., 2017). Mannini et al. compared two

integration and two machine learning approaches and found that the integration methods slightly outperformed machine learning methods (RMSE: 2.0% and 3.1% versus 2.1% and 4.2% error) (Mannini and Sabatini, 2014). Some studies reported semi-standardized routes for testing or validating their system. In these cases, the reference systems found were videos (Bussmann et al., 2004), predefined paths (Dobkin et al., 2011; Zihajehzadeh and Park, 2016), Global Navigation Satellite System (GNSS) (Perrin et al., 2000; Soltani et al., 2019), a previously validated IMU system (Brzostowski, 2018; B Fasel et al., 2017) or a measuring wheel (Schimpl et al., 2011; Supratak et al., 2018).

3.3.4 Experimental procedure

Since only validation studies were reviewed for this state-of-the-art chapter, a large majority (73%) of described experimental procedures were performed in a laboratory (Figure 28), asking the participants to walk on a treadmill, along a delimited walkway or a short corridor. Some other studies used semi-standardized settings (Ganea et al., 2012; Muhammad et al., 2018) like a predefined route around the hospital or the university including indoor and/or outdoor passage in a public area. Semi-standardized routes often include different types of floor (e.g. flat/inclined, regular/irregular, straight/curved) as mentioned previously. Very few studies validated their system in real-world settings (Brodie et al., 2015; Derungs et al., 2018; Hickey et al., 2017a). Actually, no study was found dedicated to validating a wearable system for spatial and spatiotemporal parameters estimation in a real-life situation. However, some authors tested the feasibility of their systems in real-world settings, reporting from 20h awake hours (Dobkin et al., 2011) until 14 weeks of recording (Brodie et al., 2015). For the latter, a single sensor was easily worn on the chest as a pendant by the participant, which is why they were able to monitor 14 weeks of daily-living.

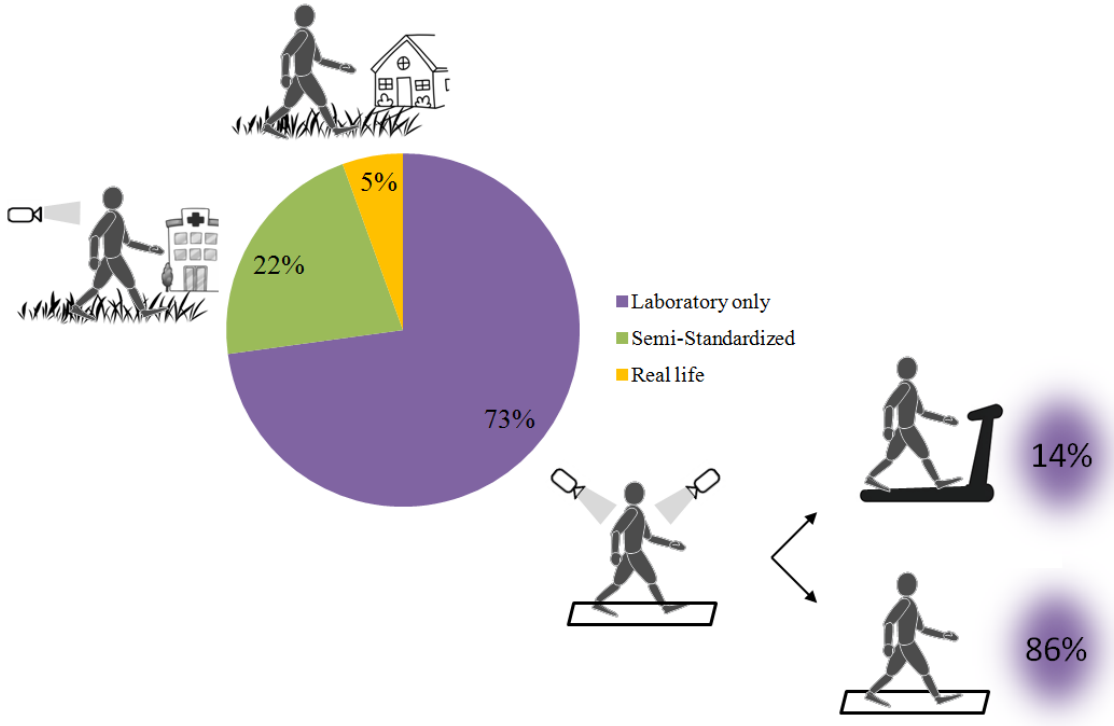


Figure 28 - Repartition of the reviewed studies regarding the experimental environments and settings

As illustrated in Figure 29, the majority (60%) of reviewed studies included only healthy participants. None of these studies were performed with children participants. Among the remaining 40%, the studies included at least one participant with a pathology affecting gait. The most studied population apart from young and healthy participants were the elderly and patients with Parkinson's Disease, both representing more than 50% of the cases (Figure 29).

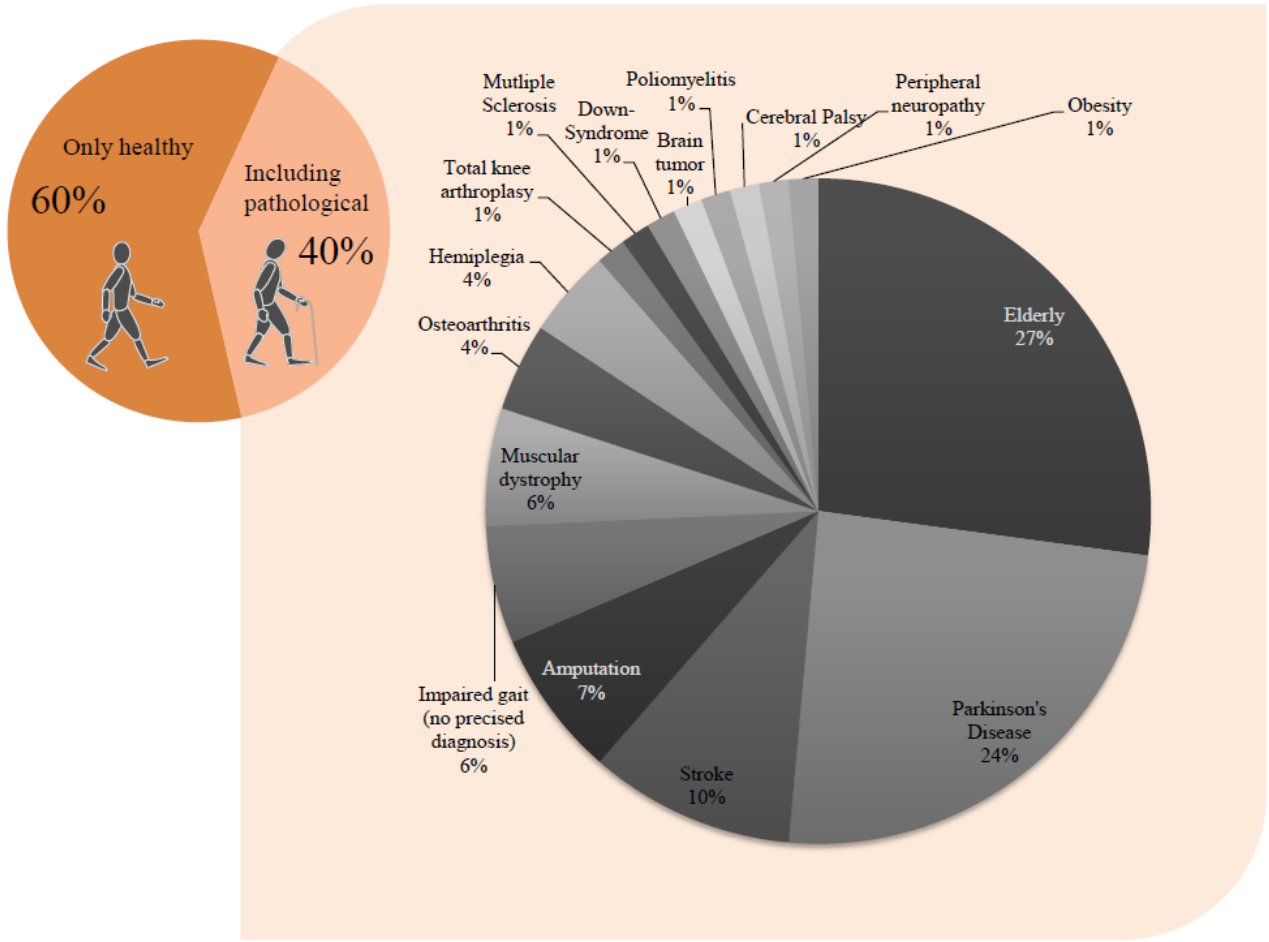


Figure 29 - Repartition of the reviewed studies regarding participants' characteristics

Tests were mainly performed at preferred self-selected speed but a large part of the reviewed studies also included a range of walking speed, fixed by the treadmill (Ben Mansour et al., 2015; Ferrari et al., 2016; Figueiredo et al., 2018), guided by a metronome (Bonomi and Salati, 2010; Selles et al., 2005), or to the participant's appreciation (slow and fast walking). The overall speed range covered in the screened articles was 0.1 (Fortune et al., 2014; McGinnis et al., 2017; Soaz and Diepold, 2016) to 2.3m/s (Anwary et al., 2018b; Doheny et al., 2010; Pepa et al., 2017). Additionally, some studies included walking tasks on inclined roads or treadmill to evaluate the impact of incline on the wearable system (Aminian et al., 1995b; B Fasel et al., 2017; Li et al., 2010; Perrin et al., 2000; Song and Kim, 2018).

3.3.5 Additional gait parameters

Computable additional parameters vary from one configuration to another. Depending on the application, some additional parameters are recommended. And this can contribute to the choice of the wearable system to use. Once temporal, spatial or spatiotemporal parameters are computed per stride, inter-stride standard deviation or coefficient of variation can be provided by the system. In fact, a lot of included studies computed the mean parameter over a trial (for example, within the studies estimating walking speed, about 60% reported the speed as an average per trial, 20% per stride and 20% per second). Those who compute their parameters per strides had the possibility to compute such metrics associated with walking regularity. Gait symmetry features can easily be provided with methods using sensors on the right and left limbs, and also, but less easily, with a single sensor configuration (Zhang et al., 2018). With sensors on the foot, other additional parameters can be computed such as the foot clearance (height during swing) (Mariani et al., 2010), the stride or swing width (Hannink et al., 2017) or foot angle (Hannink et al., 2017; Mariani et al., 2010; Nhat Hung and Soo Suh, 2013).

With sensors on the shanks and thighs, knee angle can be computed (Salarian et al., 2004). And finally, with sensors on the trunk, metrics related to upper-body stability during gait can be computed (Belluscio et al., 2019; Kosse et al., 2015). IMUs do not offer the possibility to compute the step width whereas this is clinically relevant in numerous pathological populations. However, infrared time-of-flight distance sensors (Bertuletti et al., 2019) or ultrasound sensors (Weenk et al., 2015) can be used for this purpose as they can estimate the distance between an emitter and a receiver placed on each foot, i.e. estimating the step width.

3.4 Overview and application to cerebral palsy

This review revealed that a large number of studies have been investigating the computation of STP using wearable devices for 27 years. More work has been proposed for the temporal parameters due to lower difficulties to estimate them from accelerometer or gyroscope signals. The overwhelming majority of methods exploited the detection of particular features on the signals, corresponding to specific instant of the gait cycle. This method revealed to be very promising since it is simple to implement and fits almost every possible sensor configurations (Figure 21). High accuracy was indeed found with most of the population assessed, which were mainly young healthy adults. Great challenges are however linked with the estimation of spatial parameters with wearable devices. A lot of different approaches were then proposed, including integration, biomechanical models and statistical approaches. Integration methods have the advantage to make a direct computation of the parameter but are limited by the sensor's noise and bias (Diez et al., 2018) inducing drift in the estimated continuous metrics. Integration methods may thus be recommended for short walks or for subjects having typical and regular gait patterns for which assumptions like the 'zero velocity' assumption at each step can be made to compensate the drift. This approach is also suitable for a variety of sensor configurations. Biomechanical models approach rests upon assumptions and simplifications about the body segments' displacement during gait and achieves good accuracies also for typical gait patterns. This approach is thus advocated for well defined and similar use cases and sensor configurations (Diez et al., 2018). Finally, statistical approaches have the great advantage to be suitable for any sensor configuration since many signal features that show correlation with the spatial parameter of interest can be used. However, the main drawback of these methods is the need for a large amount and a great variety of data for training to ensure good accuracy of the model. Additionally, when extensive machine learning techniques are used, no direct link can be made between the inputs and the results (black-box). Statistical approaches should thus be advised in cases where a lot of data is available and flexibility in sensor configuration is needed (Diez et al., 2018). The same concerns are related to walking speed (spatiotemporal) estimation.

We realize that none of these computational methods actually fits the cases of children with CP. Indeed, they present atypical and irregular gait patterns that prevent using assumptions necessary to reduce the drift in the integration method. Some of them present bone deformities and muscle contractures that preclude them from extending the knee for instance. Using biomechanical models simplifying the leg as a single pendulum is thus precarious. They have limited endurance as well as limited weekly availabilities to perform gait assessments so restricted amount of data is available for each patient.
Within 162 articles included in the category "description of methods", only one proposed a customized method for atypical gait patterns of patients with CP (A Paraschiv-Ionescu et al., 2019). And this study was actually from our research group, using the data generated during this doctoral work. This implies that no method has been developed or customized for this specific population prior to this thesis. However, three papers about children with CP were found within our selection of 99 studies in the category "evaluation of existing methods" (Brégou Bourgeois et al., 2014; Saether et al., 2014; Zollinger et al., 2016). Bregou-Bourgeois et al. (2014) used the method developed by Mariani et al. (2010) with two sensors on the feet (integration method) to assess

the performance of the system in children with CP (Brégou Bourgeois et al., 2014). They found a 95% level of agreement for walking speed of about 0.1m/s against an optoelectronic system. Saether et al. (2014) evaluated the difference between children with CP and with typical development regarding STP and balance parameters using the method of Moe-Nilssen et al. (1998) with a sensor at the lower back. The method used was a regression approach exploiting the quadratic relation between acceleration RMS relative to walking speed (Moe-Nilssen, 1998). No validation metrics were reported by Saether et al. (2014). Zollinger et al. (2016) measured temporal parameters using the method of Jasiewicz et al. (2006) (event detection method using anteroposterior and mediolateral acceleration signals) through two sensors, one on the waist and one on the foot, and deduced spatial parameters during a treadmill and overground tasks at fixed speed. No validation metrics were reported by Zollinger et al. (2016). Four other papers were found within our excluded articles since they did not reference the method they used, as they were mostly using commercial device and software packages. Mackey et al. assessed the reliability and validity of the intelligent device for energy expenditure and activity ('IDEEA', Minisun LLC, Fresno, CA), including five sensors located on the trunk, thighs, and feet, for the estimation of STP in children with CP. They found that the 95% limit of agreement in subject with CP was ± 0.58m/s (Mackey et al., 2008). Sivarajah et al. (2018) assessed the feasibility of the mobility-lab (APDM, Inc., Portland, OR), including 6 sensors located on the wrists, the trunk, the lower back and the shanks, to discriminate children with CP from typically developing children regarding STP. Mutoh et al. (2019, 2016) and Manikowska et al. (2013) assessed the effect of hippotherapy on STP using a sensor on the waist. In total, prior to this doctoral work, only two studies evaluated the accuracy of their system in the CP population (Brégou Bourgeois et al., 2014; Mackey et al., 2008) and they had divergent results. There is indeed a lack of validated system for the computation of gait parameters as essential as STP in the population of individuals with CP.

3.5 Limitations

An attempt of systematic literature review was carried out to present the existing methods to compute gait parameters with a wearable system. Due to large inclusion criteria, too many studies were included in this review. Thus, quality assessment of the papers was not undertaken, meaning that papers with low quality may have been included. To preclude from including papers with a very low level of significance and poor details in the description of their method, we chose to exclude case report papers and conference proceedings. Furthermore, considering the large amount of full text to read, cross-screening was not contemplated. Finally, cross-referencing was not contemplated either. All these aspects weaken the power of the review, which is why it was not considered systematic.

Additionally, several keywords could have been added in the search equation such as 'stride length', 'stride time', 'stance/swing phase' to enable absolute exhaustiveness of the review regarding temporal and spatial parameters. The choice of the equation was made in accordance with the intended publication about walking speed estimation. However, a fair and almost exhaustive overview of the previous and current practices to compute gait parameters using wearable devices was presented.

3.6 Conclusion

From 1992 to now, thousands of studies have been dedicated to the estimation of STP of gait using a wearable device, with the perspective of allowing gait analysis outside of the laboratories. Efforts were indeed made to find the most accurate solutions to compute gait STP, exploiting the IMUs' resources. We have underlined a lack of harmonization between studies regarding experimental procedures and performance evaluations. We have also highlighted the lack of validation studies in semi-free or free settings. Advantages and disadvantages of each type of approach (generalization, biomechanical assumptions, simplifications, associated sensor

configuration, etc.) are however well described and have to be considered carefully when choosing a system for a particular application. Using these methods on pathological populations such as children with CP constitutes a major challenge considering their great gait deviations. Hence, very few studies have been so far dedicated to this. Comparative studies are thus needed to be aware of the possibilities to use such devices in clinical care.

Part II

TECHNICAL STUDIES

This part includes two chapters regarding our first specific objective: To propose a tool for gait assessments in daily life fitting the specific gait deviations of children with CP in order to fill the knowledge gap about their gait performance. The choice of the system (device configuration and associated algorithms) for the assessment of gait parameters in daily life for children with CP and with TD is thus addressed in two technical studies.

The first (Chapter 4) presents the comparison of three relevant sensor configurations for the computation of spatiotemporal parameters in children with CP. This chapter drives the choice of the wearable solution that is further used in the thesis, on the basis of accuracy and precision of the three configurations as compared to the clinical reference, and patients' acceptance.

The second (Chapter 5) presents a method for gait detection in real-life settings based on a personalization set-up. A comparison between existing and personalized approaches is presented, in terms of sensitivity, specificity, accuracy and precision for walking bout detection, during a semi-standardized route outside of the laboratory.

Chapter 4 *

The choice of wearable sensors configuration to measure spatiotemporal gait parameters in children with cerebral palsy

Abstract

Wearable inertial devices have recently been used to evaluate spatiotemporal parameters of gait in daily life situations. Given the heterogeneity of gait patterns in children with cerebral palsy (CP), the sensor placement and analysis algorithm may influence the validity of the results. This study aimed at comparing the spatiotemporal measurement performances of three wearable configurations defined by different sensor positioning on the lower limbs: (1) shanks and thighs, (2) shanks, and (3) feet. The three configurations were selected based on their potential to be used in daily life for children with CP and typically developing (TD) controls. For each configuration, dedicated gait analysis algorithms were used to detect gait events and compute spatiotemporal parameters. Fifteen children with CP and 11 TD controls were included. Accuracy, precision, and agreement of the three configurations were determined in comparison with an optoelectronic system as a reference. The three configurations were comparable for the evaluation of TD children and children with a low level of disability (CP-GMFCS I) whereas the shank-and-thigh-based configuration was more robust regarding children with a higher level of disability (CP-GMFCS II–III).

* Chapter published as:

Carcreff L., Gerber C.N., Paraschiv-Ionescu A., De Coulon G., Newman C.J., Armand S., and Aminian K. " What is the Best Configuration of Wearable Sensors to Measure Spatiotemporal Gait Parameters in Children with Cerebral Palsy?", Sensors, 2018, vol. 18, num. 2 . doi: 10.3390/s18020394 – with permissions of all co-authors.

My contributions: Methodology, recruitement, investigation, software, data curation, visualization, formal analysis, writing – original draft, writing-review & editing

4.1 Introduction

Cerebral palsy (CP) is the most frequent motor disorder in children with a prevalence of 1.8:1000 births in Europe (Sellier et al., 2016). For the majority of children with CP who achieve community ambulation, an objective evaluation of their gait is necessary to accurately identify and understand gait impairments, in order to provide adequate and efficient treatment (Armand et al., 2016). Such assessments are usually performed in laboratory settings, during standardized clinical gait analysis (CGA). Numerous gait parameters including spatiotemporal parameters (STP), kinematics, kinetics, and muscle activity can be quantified using an optoelectronic (3D motion capture) system, force plates, and an electromyography system (Carcreff et al., 2016a).

During gait, foot strikes (FS) and foot offs (FO) succeed each other and constitute the base for gait cycle segmentation and the computation of STP. Gait events can be computed from a single force plate, restricting the measure to one step at a time. With the combination of several force plates and an optoelectronic system, it is possible to determine these events over several steps (Sutherland, 2002). The advantage of this method is to calculate spatial parameters, such as the stride length, directly from the marker positions. Despite its wide use in CGA (Bruening and Ridge, 2014; Desailly et al., 2009; Di Marco et al., 2017; Ghoussayni et al., 2004), the optoelectronic system has some unavoidable limitations. It suffers from inaccuracies linked to instrumental errors, soft tissue artefacts (the relative displacement between the markers and the underlying bone), and marker misplacement due to anatomical landmark palpation difficulties (Di Marco et al., 2017). Since STP estimation is mainly based on the tracking of markers located on the heels and toes, soft tissue artefacts and marker misplacement are not likely to induce major errors. Therefore, instrumental errors are the main sources of inaccuracy in this situation. In 2005, a review reported mean errors for marker distance estimates between 0.1 mm and 5.3 mm depending on the systems (Chiari et al., 2005). Thanks to the improvement in camera resolution, these errors were expected to decrease. Recently, Di Marco et al. reported that the number of cameras, the calibration volume, and the calibration procedure can induce errors in the marker trajectories reconstruction between 0.2 mm and 1.7 mm (Di Marco et al., 2017, 2015). Moreover, the optoelectronic system restrains the measurement volume to the laboratory and thus may hinder the patient's natural gait. As a result, gait parameters obtained through CGA are not fully representative of the usual and daily walking habits (described as 'performance' (World Health Organization, 2002)) of children with CP (Holsbeeke et al., 2009; Smits et al., 2014; Van Eck et al., 2009). Performance can currently be estimated through questionnaires and clinical observations which have the inherent drawback of being subjective and evaluator-dependent, and thus associated with potential bias (Keawutan et al., 2014; Olivier et al., 2015). Therefore, there is a need to objectively assess gait performance in daily-life conditions in order to complement CGA, thus enhancing therapeutic choices for children with CP based on real-life data. Wearable inertial sensors can be used to fulfill this need.

Inertial sensors are microelectromechanical systems, including accelerometers and gyroscopes, contained in small casings that can be carried by the patient without restrictions for several hours of measurements. A wearable sensor-based gait analysis system relies on a sensor configuration and an associated algorithm. Many sensor configurations have been tested for STP estimation varying in numbers of sensors (single or multiple), type (single or triaxial), and location on the body (Yang and Li, 2012a). As, in human gait, most body motion comes from the lower limbs, sensors are commonly fixed on the lower limbs (Yang and Li, 2012a). Gait events are detected according to specific features appearing on accelerometer and gyroscope signals in the time and frequency domains (Aminian et al., 2002; Boutaayamou et al., 2017; Khandelwal and Wickström, 2017). Spatial parameters are computed from these signals through methods dependent on the sensor location (Aminian et al., 2002; Yang and Li, 2012a). Yang et al. defined three categories of algorithms: the abstraction

models where the spatial parameter is estimated from a black box model building the relationship between the sensor measurements and the output (e.g., artificial neural networks, third-order polynomial model, etc.); the human gait models which use the geometric properties of the lower limbs to estimate stride length; and the direct integrations which consist of integrating the acceleration in the global frame between two specific points of the gait cycle in order to calculate stride velocity (simple integration) and stride length (double integration). The validity of gait event detection and STP computation from wearable devices has been studied in healthy adults, adults with disease, or elderly population, but scarcely in children (Esser et al., 2011; Mansour et al., 2015; Trojaniello et al., 2014; Zijlstra and Hof, 2003). Lanovaz et al. found that, in healthy children, a system of six inertial sensors was valid for temporal detection but showed consistent bias for spatial parameters estimation with the gait model method (Clifton et al., 1982). In children with CP, a protocol named "Outwalk" has been developed to measure trunk and lower-limb 3D kinematics using an inertial and magnetic measurement system, but the authors did not assess STP (Cutti et al., 2010; Van Den Noort et al., 2013). Laudanski et al. observed that gait analysis based on sensors on the feet bring more error than shank-mounted sensors, especially for abnormal gait pattern such as toe-out walking (Laudanski et al., 2011). In children with CP with low to mild gait impairments, Bregou-Bourgeois et al. used two foot-worn inertial sensors and the direct integration method to estimate STP and showed good accuracy, precision, and agreement against an optoelectronic system for the estimation of stride length, walking speed, and foot angles with regard to the ground (Brégou Bourgeois et al., 2014). These previous studies pointed out the difficulty of assessing gait in children with CP with inertial sensors since these children cannot achieve the expected movement properly (i.e., full foot contact during gait (Brégou Bourgeois et al., 2014), good alignment in static, or pure flexion/extension of the knee for functional calibration of the sensor axes (Van Den Noort et al., 2013)). Considering these challenges and since gait patterns are very heterogeneous among patients with CP who are able to walk (Armand et al., 2016), the usability of other sensor set-ups deserves exploration in order to determine which is the most appropriate one. Furthermore, children with a higher level of impairment should be considered as they may benefit even more from the assessment of their gait performance.
The aim of this study was to evaluate and compare the measurement performance of three wearable configurations and to identify the most appropriate set-up for gait assessment of children with CP. For this purpose, a standard optoelectronic system was used as a reference to evaluate event detection and STP computation.

4.2 Materials and methods

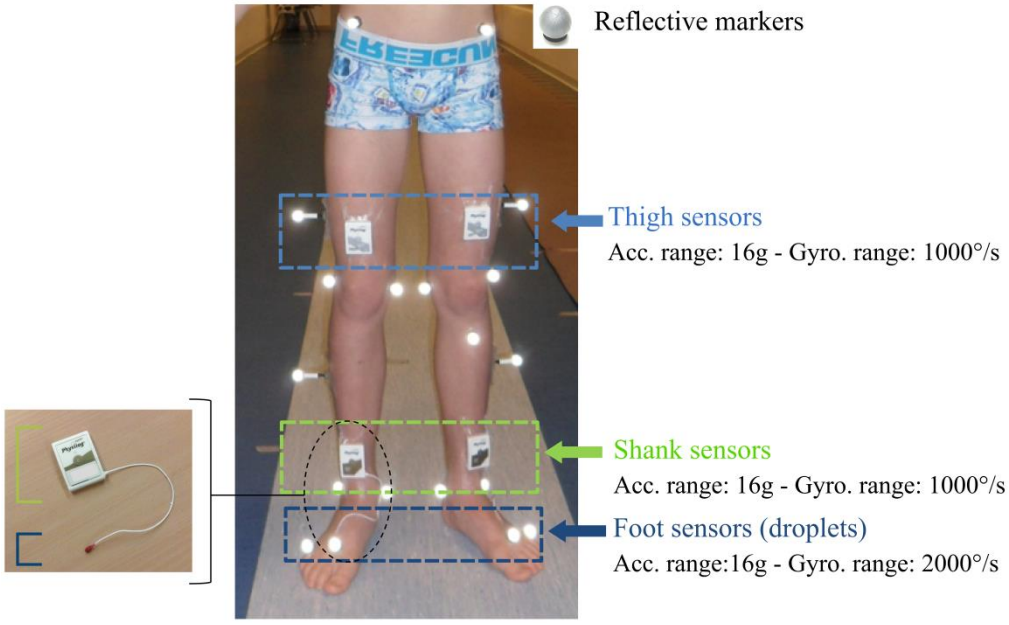
This study was an observational case-control validation study with a single center setup.

4.2.1 Participants

Fifteen children and adolescents with CP and eleven age- and sex-matched typically developing (TD) controls were evaluated in the laboratory of kinesiology within Geneva University Hospitals (HUG). Participants of the CP group were recruited from the patients followed at the HUG pediatric orthopedics unit if they met the following inclusion criteria: (a) aged between 8 and 20 years; (b) diagnosis of CP; (c) ability to walk in the community with or without mechanical walking aids; and (d) with a level of Gross Motor Function Classification System (GMFCS) (Palisano et al., 1997) between I and III. For the control group, children were recruited among collaborators' or patients' acquaintances. The exclusion criteria for both groups were those that precluded adequate participation in the measurement sessions (mental age <8 years, severe visual disorder, attention deficit, and other significant behavioral issues). All participants provided written consent, and the protocol was approved by the hospital's institutional ethical committee (CCER-15-176).

4.2.2 Protocol

A trained experimenter measured the following anthropometric data: leg, thigh, shank, and foot lengths, as well as knee, ankle, and pelvis widths which were required inputs for the computation of gait parameters (by the optoelectronic and the wearable systems). Participants were subsequently equipped with the equipment described below, as illustrated in Figure 30 (all sensor configurations were worn at the same time), and asked to walk barefoot on a 10-m walkway. They walked at their self-selected speed for six to eight trials, in order to record a sufficient quantity of gait cycles per participant (minimum of 60 cycles). Participants with a high level of disability (GMFCS III) were allowed to perform the evaluation with their mechanical aid (e.g., walker).



Feet sensors are embedded in a droplet (red PCB resin on the picture on the left), corresponding to deported 6D inertial units connected to the shank sensors.

Figure 30 - Equipment on the participant's lower limbs: reflective markers for the optoelectronic system and inertial Physilog sensors for the wearable configurations on the thighs, shanks, and feet

4.2.3 Reference spatiotemporal parameters of gait using laboratory setting

4.2.3.1 Equipment

A set of 35 reflective markers (14 mm diameter) was placed on specific anatomical landmarks of the participant's head, trunk, pelvis, arms, thighs, shanks, and feet according to the full-body Plug-In-Gait model (Davis, 1991) (Figure 30). Leg lengths, pelvis, knee, and ankle widths previously measured were used as inputs in the Plug-In-Gait model. Marker trajectories were recorded by a twelve-camera optoelectronic system (Qualisys Motion capture systems, Göteborg, Sweden) set at a sampling frequency of 100 Hz. Two force plates (AMTI Accugait, Watertown, NY, USA) embedded in the middle of the walkway recorded ground reaction forces at 1000 Hz.

4.2.3.2 Spatiotemporal parameters computation

As it is the clinical standard for in-laboratory gait analysis, the force plates and optoelectronic systems were set as reference to compare the three wearable configurations (Caldas et al., 2017; Veilleux et al., 2016). When an entire foot contact on the force plate was available, the gait events (FS and FO) were determined from the vertical ground reaction force based on a threshold sets to 20 N. The subsequent occurrences of the same events were detected on the marker trajectories by the kinematic-based model (Stanhope et al., 1990). All rated events

were manually checked frame by frame on the sagittal view of the heel and toe markers in the MOKKA software (Barré and Armand, 2014). The stride time was calculated as the time difference between two successive FS, the stride length was computed as the distance separating the heel markers at two successive FS times, and the stride velocity was calculated as the stride length divided by the stride time for each gait cycle (Hollman et al., 2011).

4.2.4 Spatiotemporal parameters of gait using wearable setting

4.2.4.1 Equipment

Six synchronized inertial sensors (Physilog4®, Gait Up, Renens, Switzerland) were used in this study. Physilog4® is a standalone device (dimensions: 50 mm × 37 mm × 9.2 mm, weight: 19 g) comprising a triaxial accelerometer, triaxial gyroscope, triaxial magnetometer, and barometer with adjustable ranges, battery, a memory unit, and microcontroller. The magnetometer and barometer were disabled. The sampling frequency was set at 100 Hz. Sensors were fixed on the participant's thighs, shanks, and feet bilaterally using a hypoallergenic adhesive film (Opsite Flexigrid, Smith & Nephew Medical, Hull, UK), as shown in Figure 30. Sensors on the feet were embedded in a droplet (a small deported 6D sensor unit containing the 3D accelerometer and 3D gyroscope) in order to be appropriate for measuring activities in daily life settings: either barefoot or with shoes. Shank and thigh sensors were always oriented in the same way relating to the thigh and the shank, as shown in Figure 30.
The optoelectronic and wearable systems were synchronized using an additional Physilog4® receiving a trigger signal from one camera for every trial start and stop. The synchronization was performed in post-treatment according to the pulse train recorded by the additional sensor.

4.2.4.2 Sensor configuration and associated algorithm

Three configurations were chosen, which all have the following in common: (1) algorithms described in research studies with high number of subject (n > 800) (Dadashi et al., 2013; Rochat et al., 2010; Seematter-Bagnoud et al., 2011), (2) commercially available sensors, (3) easy to setup sensors and possibility of long-term measurements in daily-life, and (4) validation against laboratory system in adult populations (healthy or with disease). The three configurations use different sensor locations: first, the 'Shanks and Thighs' (ShTh) with four sensors fixed on both thighs and shanks; second, the 'Shanks' (Sh) with only one sensor on each shank; and finally, the 'Feet' with one sensor on each foot. The algorithms associated to the three above-mentioned configurations were used in this study: the double pendulum gait model in ShTh (Salarian et al., 2004) and Sh, with a reduced number of sensors in Sh (Salarian et al., 2013), and the direct integration method in Feet (Mariani et al., 2013b, 2010). The ShTh and Sh methods have the same algorithm for gait event detection. Table 6 provides details about the three configurations regarding sensor location, algorithms, event detection, output gait parameters, and information about validation of the algorithms.

4.2.5 Data analysis

Two gait events, FS and FO, as well as three STP, stride time, stride length, and stride velocity, were extracted from the three wearable configurations for each participant and each side, and compared cycle by cycle with the same outputs extracted from the reference (optoelectronic system). These parameters were selected as they are fundamental descriptors of gait and the computation of other STP parameters is based on them.
For TD participants, the parameters extracted from left and right sides were congregated since there was no difference between limbs. For children with CP-GMFCS I, the parameters were separated into paretic and non-

paretic limbs according to their clinical profiles. Children with CP-GMFCS II and III were all bilaterally affected and, therefore, left and right sides were congregated and reported as paretic limbs.
The number of non-detected gait cycles, resulting from irregularities in the signal pattern (mostly due to pathological gait), was reported for each method. In cases where gait events were detected but no associated STP was computed, the cycle was not considered and reported as non-detected.

4.2.6 Statistical analysis

We conducted descriptive analyses to evaluate the consistency of the three configurations with regard to the reference system. To that purpose, error (mean and standard deviation of the difference with the reference) was determined for each configuration. Regarding gait event detection, positive/negative values stand for late/early gait event detection, respectively, and over/underestimation of STP. The analyses were performed for the subgroups of TD, CP-GMFCS I (subdivided into paretic and non-paretic sides), and CP-GMFCS II and III in order to observe the influence of the impairment level on the error.
Spearman's correlation coefficients (r) were used to evaluate the linear association between each configuration and the reference for the three STP in each subgroup. Furthermore, to quantify the agreements between each configuration and the reference system and visually represent the distribution of the errors, a graphical analysis through Bland–Altman plots was performed for each configuration for the three STP for each group.

Table 6 - Description of the three wearable configurations: Shanks-and-Thighs ('ShTh'), Shanks ('Sh'), and Feet according to the sensors placement and associated algorithms

	Configuration Name	Shanks and Thighs	Shanks	Feet	
	Abbreviation	ShTh	Sh	Feet	
Sensor placement		On the anterior side of each shank and thigh	On the anterior side of each shank	On top of each foot	
Associated algorithm	Authors	(Salarian et al., 2004)	(Salarian et al., 2013)	(Mariani et al., 2013b, 2010)	
	Calibration on sensor axis	No calibration needed as the pitch axis is assumed systematically aligned with the mediolateral axis of the body		Sensor axes vertically aligned using the gravity component during motionless periods and the orientation was obtained by maximizing the pitch angular velocity of the foot throughout the gait trial.	
	Events (temporal) detection method	Peak detection on pitch angular velocity of shanks		Peak detection on pitch angular velocity and norm of acceleration of feet	
	Spatial detection method	Application of a double pendulum model (Aminian et al., 2002) from shank and thigh angles (calculated by integration of shanks and thigh angular velocities) and segments lengths.	Application of a double pendulum model (Aminian et al., 2002) from shank and thigh angles estimated only from shanks angular velocities and segments lengths. Thigh angles estimated from shank angles using Fourier series and least square optimization.	De-drifted double integration of gravity-free acceleration between two successive and identical events (foot flat)	
	Spatiotemporal computation	Temporal parameter divided by spatial parameter		De-drifted single integration of gravity-free acceleration between two successive and identical events (foot flat)	
	Outputs gait parameters	n = 24; includes: - Gait event times (foot strike (FS), foot off (FO)) - Temporal parameters (cadence, stride time, swing time, stance time, …) - Stride length, stride velocity - Shank, thigh and knee angle range of motion - Maximal peak angular velocity of shank		n = 55; includes: - Gait event times (FS, FO) - Temporal parameters (cadence, stride time, swing time, stance time, …) - Stride length, stride velocity - Turning angle - Foot clearances features, foot angles at FS, FO	
	Population used for validation	Healthy adults, elderly, patients with a total hip replacement, patients with coxarthrosis (Aminian et al., 2002; Najafi et al., 2009), and Parkinson's disease (PD) adults (Salarian et al., 2004)	Healthy adults, patients with a total hip replacement, patients with coxarthrosis, and PD patients (Salarian et al., 2013).	Young, elderly adults and PD patients (Mariani et al., 2013a, 2010)	Children with cerebral palsy (CP) (Brégou Bourgeois et al., 2014)
	Mean errors (±sd) against reference	Against force plate and optoelectronic system (ELITE, BTS, Milan, Italy) - Stride time: 0.002 (±0.023) s - Stride length: 0.035 (±0.085) m - Stride velocity: 0.030 (±0.076) m/s Against Instrumented walkway (GaitRite, Franklin, USA): - Stride time: 0.013 (±0.020) s - Stride velocity: 0.04 (±0.07) m/s	Against force plate and optoelectronic system (ELITE, BTS, Milan, Italy) - Stride time: 0.002 (±0.023) s - Stride length: 0.038 (±0.066) m - Stride velocity: 0.038 (±0.056) m/s	Against force plate and optoelectronic system (Vicon, Oxford Metrics, Oxford, UK) - Stride length: 0.034 (±0.046) m - Stride velocity: 0.043 (±0.042) m/s For PD adults: - Stride length: 0.013 (±0.030) m - Stride velocity: 0.028 (±0.024) m/s	Against force plate and optoelectronic system (Vicon, Oxford Metrics, Oxford, UK) - Stride length: 0.040 (±0.052) m - Stride velocity: 0.051 (±0.048) m/s

4.3 Results

Characteristics of the study population are summarized in Table 7. In total, 2395 cycles (TD: 998, CP-I: 747, CP-II-III: 650) were analyzed with ShTh and Sh, and 2099 cycles (TD: 934, CP-I: 681, CP-II-III: 484) with Feet. The corresponding cycles were selected for the reference system. No false positive gait events were detected. The number of non-detected cycles is shown inTable 8. Feet missed five cycles and ShTh/Sh missed three cycles for the TD group. Feet missed 197 cycles and ShTh/Sh missed 58 cycles for the CP group. Feet did not detect any events for one participant who walked exclusively on his toes.

Table 7 - General characteristics of the study population

	TD	**CP**	
N	11	15	
		GMFCS I	**GMFCS II-III**
		7	8
		Unilateral	Bilateral
		5	10
Sex Number of girls in the group (%)	5 (45)	8 (55)	
Age in years mean ± std	13.5 ± 2.9	12.8 ± 3.1	

Table 8 summarizes the errors in estimating FS and FO times from the three configurations against the reference. Figure 31 illustrates an example for each group of FS and FO detection with ShTh/Sh and Feet configurations as compared to the reference. The three configurations showed similar errors for FS detection within the TD and the non-paretic groups (errors < 0.042 ± 0.030 s). Feet showed a higher error in detecting FS for the paretic groups (0.051 ± 0.053 s for GMFCS I and 0.077 ± 0.299 s for GMFCS II-III) compared to ShTh/Sh (0.037 ± 0.051 s for GMFCS I and 0.053 ± 0.048 s for GMFCS II-III). The error of FO detection was lower compared to FS detection, for the three configurations and the whole population (|errors| < 0.029 ± 0.058 s for FO and |errors| < 0.077 ± 0.299 s for FS).

Table 8 also reports the errors for STP computations (stride time, stride length, and stride velocity). The error of all configurations was inferior to 0.003 ± 0.072 s for stride time estimation within each group, except for the CP-GMFCS II-III group with Feet (0.012 ± 0.129 s). Feet showed lower errors compared to the two other configurations for stride length estimation, for all the groups except the CP-GMFCS I paretic group where the errors were equivalent between ShTh and Feet (0.019 ± 0.066 m and 0.018 ± 0.069 m). The highest errors for stride length estimation were found with Sh in each group. For stride velocity, ShTh showed lower errors for the CP groups (e.g., 0.024 ± 0.118 m/s (ShTh) against −0.127 ± 0.133 m/s (Sh) and 0.073 ± 0.123 m/s (Feet) in the GMFCS II-III group), whereas lower errors were found with Feet for the TD group (0.030 ± 0.045 m/s (Feet) against 0.073 ± 0.067 m/s (ShTh) and 0.133 ± 0.091 m/s (Sh)).

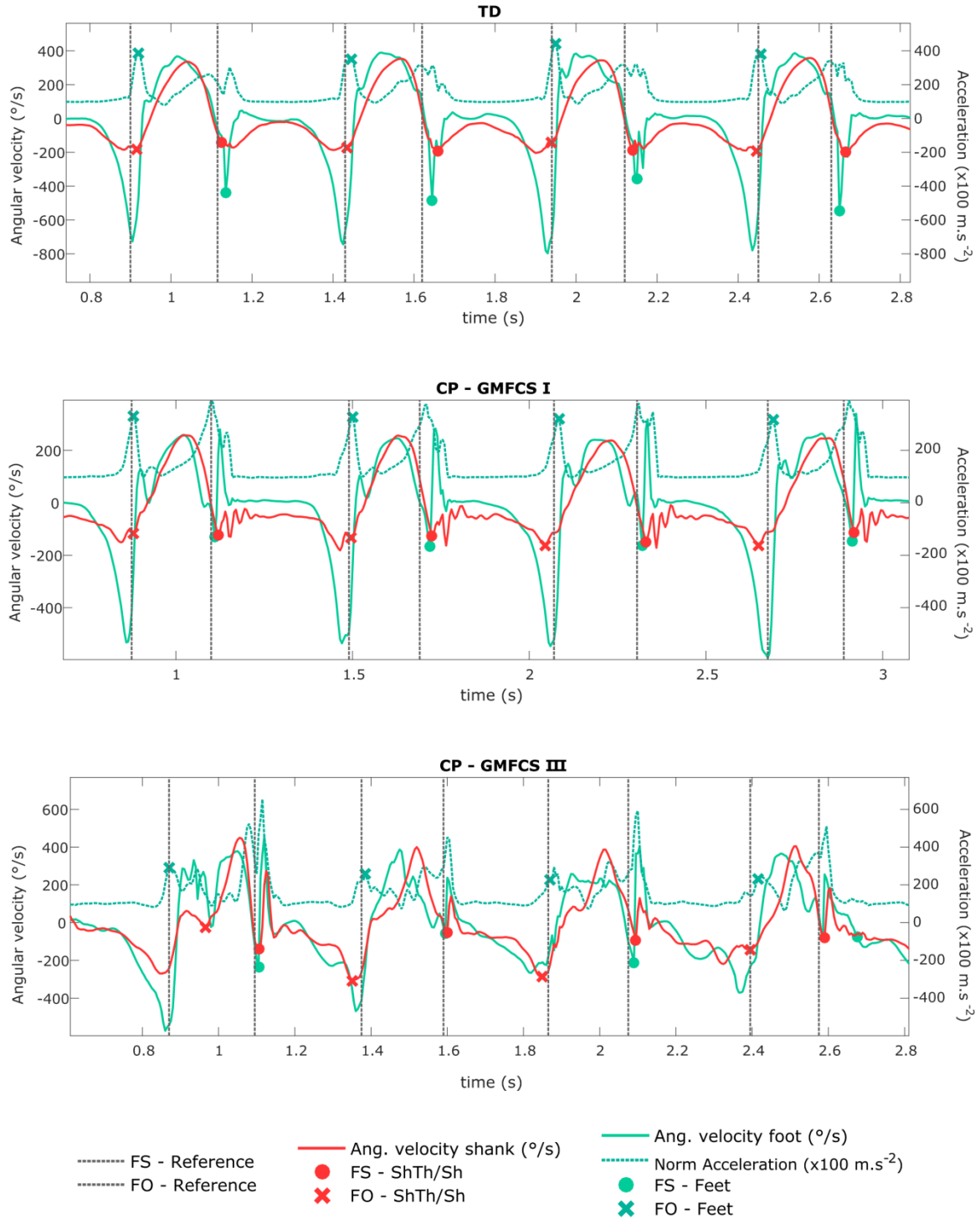
Figure 32 presents the cycle-by-cycle comparison between each configuration and the reference for the three STP and the different groups. All correlations were significant ($p < 0.05$). Correlation coefficients were high to very high ($r > 0.7$) according to previous recommendations (Mukaka, 2012) for the three configurations except for stride length estimation in the CP-GMFCS II-III group with ShTh and Sh where the correlation coefficients were moderate ($r = 0.545$ and $r = 0.576$ respectively).

The agreement assessed by Bland–Altman plots is shown in Figure 33. Higher levels of agreement were found for ShTh/Sh compared to Feet for stride time detection in CP-GMFCS I (0.095 s against 0.053 s) and CP-GMFCS II-III (0.252 s against 0.142 s). However, a higher agreement was reported with Feet for stride length in all groups as compared to the two other configurations. For the stride velocity, a better agreement was found with Feet for the TD and the CP-GMFCS I groups (0.088 m and 0.121 m/s) as compared to ShTh (0.134 m 0.0.133 m/s) and Sh (0.179 m and 0.207 m/s); however, ShTh showed a better agreement for CP-GMFCS II-III (0.232 m/s) as compared to Feet (0.242 m/s) and Sh (0.260 m/s).

Table 8 - Number of non-detected cycles, mean values (and standard deviation), mean errors (and standard deviation) against the optoelectronic system for gait event (Foot strike and Foot off) detection and spatiotemporal parameters (stride time, stride length, and stride velocity) computation

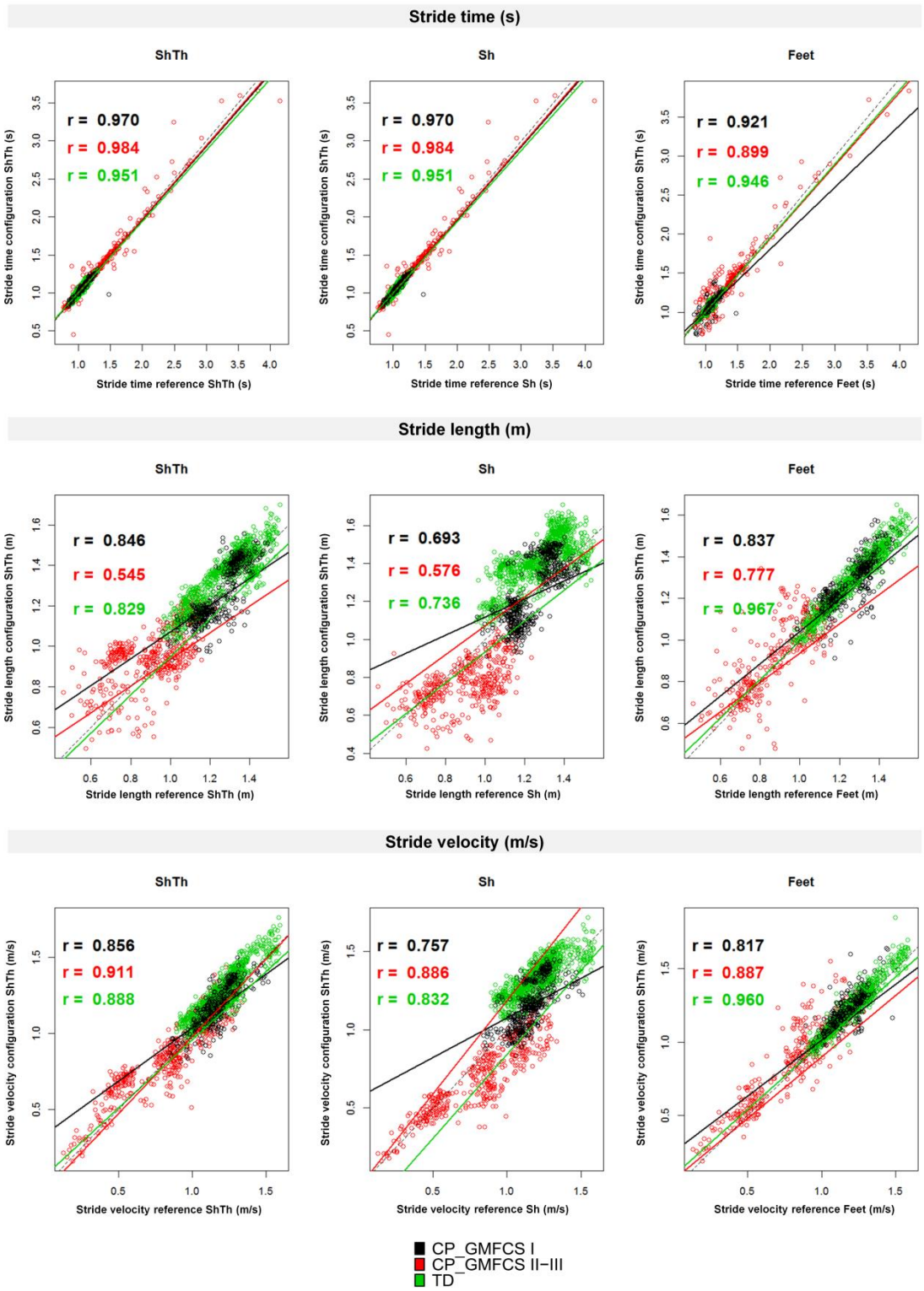
		TD		CP					
				GMFCS I				GMFCS II-III	
		Healthy sides		Non-paretic side		Paretic side		Paretic sides	
Cycle detection		*n* (%)		*n* (%)		*n* (%)		*n* (%)	
Number of non-detected cycle	ShTh/Sh	3 (0.1)		0 (0.0)		0 (0)		58 (2.4)	
	Feet	18 (0.8)		24 (1.0)		3 (0.1)		170 (7.4)	
Gait event		Error mean (SD)		Error mean (SD)		Error mean (SD)		Error mean (SD)	
Foot strike (s)	ShTh/Sh	0.040 (0.021)		0.042 (0.030)		0.037 (0.051)		0.053 (0.048)	
	Feet	0.047 (0.020)		0.048 (0.020)		0.051 (0.053)		0.077 (0.299)	
Foot off (s)	ShTh/Sh	−0.011 (0.021)		−0.004 (0.029)		−0.008 (0.045)		−0.011 (0.063)	
	Feet	0.012 (0.021)		0.014 (0.018)		0.020 (0.018)		0.029 (0.058)	
STP		Mean (SD)	Error mean (SD)	Mean (SD)	Error mean (SD)	Mean (SD)	Error mean (SD)	Mean (SD)	Error mean (SD)
Stride time (s)	**Reference**	**1.061 (0.080)**		**1.095 (0.073)**		**1.055 (0.092)**		**1.197 (0.388)**	
	ShTh/Sh	1.064 (0.082)	0.000 (0.023)	1.091 (0.090)	0.001 (0.017)	1.055 (0.091)	0.000 (0.031)	1.200 (0.393)	0.003 (0.072)
	Feet	1.061 (0.083)	0.000 (0.022)	1.096 (0.073)	0.001 (0.019)	1.052 (0.101)	0.000 (0.057)	1.312 (0.431)	0.012 (0.129)
Stride length (m)	**Reference**	**1.276 (0.144)**		**1.267(0.108)**		**1.242 (0.104)**		**0.896 (0.161)**	
	ShTh	1.351 (0.135)	0.075 (0.069)	1.297 (0.145)	0.030 (0.078)	1.262 (0.134)	0.019 (0.066)	0.942 (0.143)	0.046 (0.140)
	Sh	1.420 (0.133)	0.144 (0.098)	1.298 (0.179)	0.031 (0.124)	1.269 (0.157)	0.027 (0.104)	0.770 (0.118)	−0.126(0.137)
	Feet	1.295 (0.151)	0.025 (0.037)	1.296 (0.095)	0.023 (0.036)	1.257 (0.118)	0.018 (0.069)	0.916 (0.182)	0.039 (0.118)
Stride velocity (m/s)	**Reference**	**1.201 (0.155)**		**1.167 (0.110)**		**1.184 (0.104)**		**0.810 (0.283)**	
	ShTh	1.277 (0.154)	0.073 (0.067)	1.193 (0.129)	0.026 (0.072)	1.201 (0.129)	0.018 (0.065)	0.834 (0.252)	0.024 (0.118)
	Sh	1.338 (0.115)	0.133 (0.091)	1.193 (0.160)	0.025 (0.116)	1.208 (0.143)	0.024 (0.098)	0.683 (0.212)	−0.127 (0.133)
	Feet	1.233 (0.165)	0.030 (0.045)	1.200 (0.093)	0.036 (0.039)	1.216 (0.117)	0.035 (0.070)	0.831(0.286)	0.073 (0.123)

Positive/negative values stand for late/early gait event detection respectively and over/underestimation of STP. Reference values are in bold.



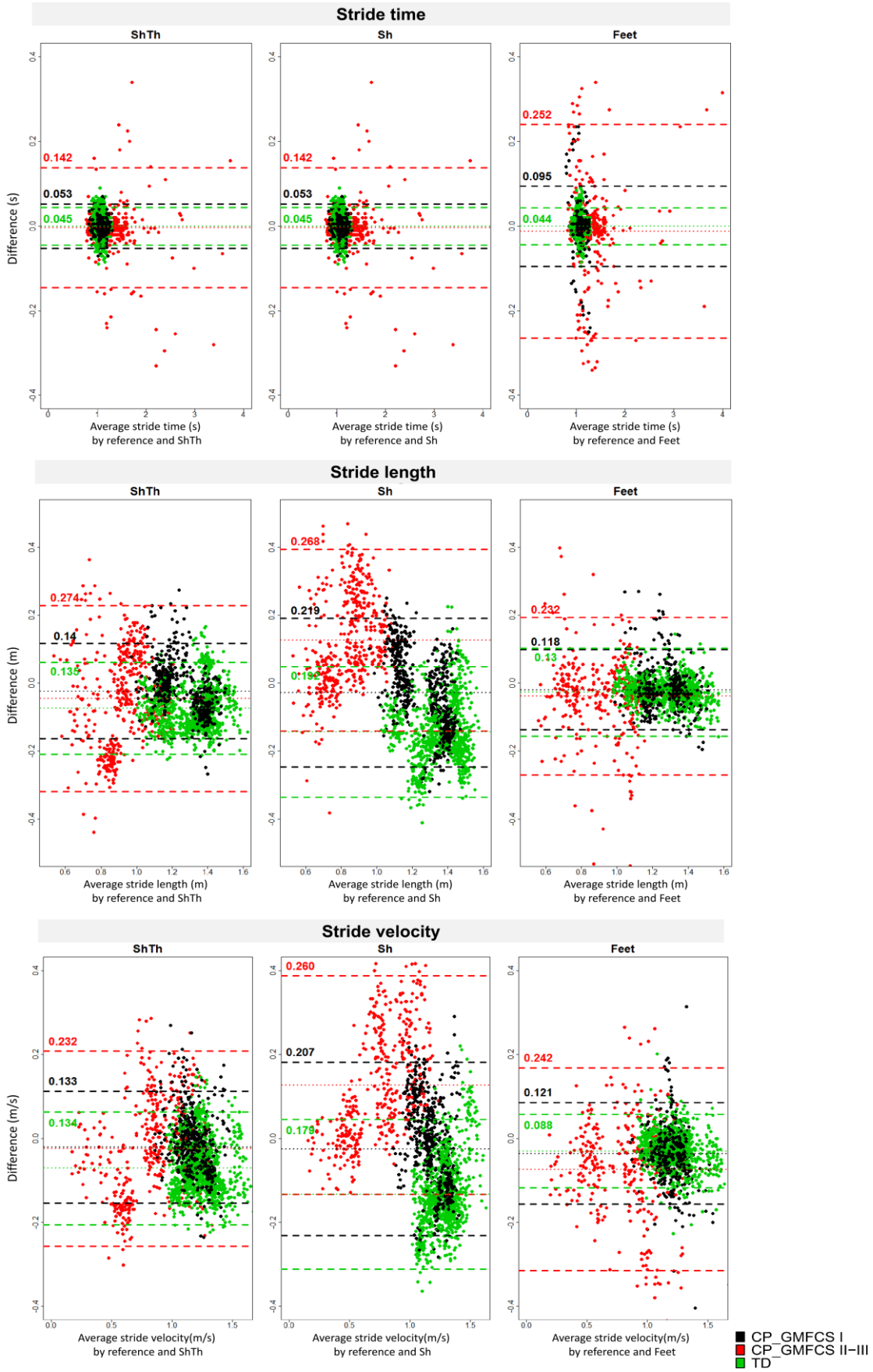
The gait events (FS and FO) detected by the wearable configurations are shown by the symbols on the corresponding signals. The vertical lines define FS and FO detected by the reference. Four strides are represented for each example, corresponding to a typically developing (TD) child, a child with CP-GMFCS I, and a child with CP-GMFCS III.

Figure 31 – Gait events detection represented on the shank angular velocity, the foot angular velocity and the norm of acceleration signals (measured by the wearable configurations ShTh/Sh and Feet) according to the method



Spearman's correlation coefficients are reported. Dashed lines represent y = x. Green: TD; Black: CP-GMFCS I level; and Red: CP-GMFCS II-III levels.

Figure 32 - Correlations between the wearable configurations (Shanks-and-Thighs 'ShTh', Shanks 'Sh', and Feet) and the optoelectronic system for the three spatiotemporal parameters (stride time, stride length, and stride velocity)



Mean error and level of agreement (±1.96 standard deviation) are represented by horizontal lines. Green: TD; Black: CP-GMFCS I level; and Red: CP-GMFCS II-III levels.

Figure 33 - Bland–Altman plots of the three wearable configurations (Shanks-and-Thighs 'ShTh', Shanks 'Sh', and Feet) against the optoelectronic system for the three spatiotemporal parameters (stride time, stride length, and stride velocity)

4.4 Discussion

In this study, we aimed to compare three wearable configurations defined by different sensor positioning and associated algorithms in order to choose the most appropriate one for gait performance evaluation in children with CP. The main findings were that the configuration using sensors only on the shanks was not appropriate for the spatial and spatiotemporal estimation for the whole study population, and ShTh and Feet provided advantages depending on the estimated parameter and the level of severity of the child. Indeed, temporal parameters were better estimated by the ShTh configuration in the pathological groups, whereas spatial parameters were better estimated by the Feet configuration. For velocity estimation, the Feet configuration was better in TD children and children with a mild gait impairment (GMFCS I), but the ShTh configuration was better in children with more impaired gait (GMFCS II and III).

4.4.1 Temporal detection

The key starting point of gait analysis is the segmentation of gait episodes into gait cycles using specific temporal events: FS and FO. For the whole study population, the three configurations were comparable regarding the detection of these events, with ShTh and Sh being more robust than Feet to detect events in challenging gait patterns (less non-detected cycles and better FS detection in the CP group compared to Feet). When discussing the temporal results, one has to consider that the resolution frame of both systems was 0.01 s (sample frequency: 100 Hz), that the reference system error can reach 0.02 s (Stanhope et al., 1990), and that the systems' synchronization precision was up to 0.01 s due to the delay between the trigger signal recorded by the additional Physilog and the actual start of the cameras. Considering these statements, FO detection with wearable systems was very close to FO detection of the reference (1 to 3 frames difference). For FS detection, the difference between the systems was larger (superior to 3 frames) especially for Feet for the most severely affected patients (up to 7 frames difference), indicating that ShTh/Sh was more accurate to segment gait trials and therefore appropriate to estimate the stride time for these patients. The errors of FS time related to the ShTh method in TD children was five times higher than those of the original method found by Salarian et al. including Parkinson's disease and healthy adults (Salarian et al., 2004). This could be due to the difference in reference event detection or sampling frequency of the inertial sensors twice higher than in the present study. The difficulty to detect events with inertial sensors is directly linked to, first, the pattern of the signal and, second, its smoothness. As illustrated in Figure 31, in abnormal gait patterns, expected features of the signal (such as specific thresholds, time windows, or peaks) can be missing, and non-expected features (such as extra-peaks) can appear which decrease the algorithm performance for event detection. In CP, these abnormal patterns are found especially at the distal parts of the limbs (at feet level) since movements of the distal limbs are more affected by the pathology than the proximal segments (Berker and Yalçin, 2008). This explains why ShTh seems preferable for children with a high level of disability for gait events detection.

4.4.2 Spatial detection

The Sh configuration was not suitable for children. Sh errors were between 3.5 and 3.8 times higher in our study compared to previously published results for healthy adults (Salarian et al., 2013). Indeed, with Sh, we found a systematic error for TD (11% of mean stride length) and CP-GMFCS II-III groups (14% of mean stride length). The Sh method uses a thigh predictor to estimate the thigh angles for stride length computation which has been trained on adults data (healthy and Parkinson's disease patients). Even if the method aimed to suit any target population (Salarian et al., 2013), it proved unfit for the children population, even the TD children. Furthermore, as the thigh angle is predicted from the shank sensor, misalignment of the sensor axis with the mediolateral axis of the shank has a greater impact on Sh results compared to the results where both thigh and shank angles are estimated from the thigh- and shank-fixed sensors. A calibration procedure that aligns the

sensor frame with the anatomical frame of the shank would probably increase the performance of the system (Salarian et al., 2013). Such a calibration was not performed in this study as it was not straightforward for the heterogeneous and highly affected children we evaluated. The focus of this paper was the evaluation of errors before any calibration.

Previous studies found that STP computation with inertial sensors in healthy populations was improved when the sensors were closer to the ground (Iosa et al., 2016; Washabaugh et al., 2017) (i.e., closer to the measure). The results of this study partially confirmed this since Feet was found more accurate in average to estimate stride length compared to ShTh. On the other hand, Feet configuration was not able to analyze one toe-walking participant. Indeed, the Feet method is based on the assumption that the participant achieves 'foot-flat' contact at mid-stance to set the initial orientation of the sensor relative to the fixed frame (Mariani et al., 2010). This condition was not fulfilled for all children with CP included in this study, especially in the GMFCS II-III group, which caused the decreased performance of the algorithm. Overall, Feet configuration might be more accurate for STP parameters but is limited for highly abnormal gait patterns, which are more accurately estimated with sensors on shanks and thighs.

Finally, both ShTh and Feet configurations reported errors lower than the in-laboratory intra-subject variability of gait in children (Steinwender et al., 2000), so they can both be considered as valid and suitable for gait assessments.

4.4.3 Choice for daily life assessment

The main perspective of this study is to determine the optimal configuration of sensors for the assessment of gait in the daily-life of children with CP. While measurement errors were the main criteria of comparison between the three systems, other aspects require careful consideration when choosing the best set-up for daily-life application.

On one hand, it is useful to keep the number of sensor units as low as possible to increase comfort for the patient, decrease the set-up time, and thus, make the system acceptable for long measurements (Hegde et al., 2016). Feet sensors were embedded in a droplet fixed directly on the skin to be independent of shoe wearing in order to allow the monitoring of all gait episodes within a day, including various environments. However, this system sometimes provided discomfort when tested outside the laboratory, because the shoe pressuring on the sensor droplet caused pain. Even if the shank and thigh sensors were larger, they did not hinder the children's gait and were more convenient. However, the positioning of sensors on the shanks might need to be adapted for the children while wearing orthoses. On the other hand, more sensors can detect a higher variety of gait parameters and activities which confer a substantial advantage for daily life assessment (Attal et al., 2015; Paraschiv-Ionescu et al., 2012). ShTh configuration allows the recognition of the sitting, lying, and standing posture whereas Feet configuration cannot distinguish sitting from standing posture. Computation of complementary parameters, valuable for the assessment of children with CP, must also be considered. For example, foot clearance and foot/floor angles can be computed only with the Feet configuration, and knee angle only with the ShTh method.

Combining these practical aspects with the accuracy of the measurements, we selected the configuration using shank and thigh sensors for further testing of its usability for long-term assessments in laboratory-free conditions.

4.4.4 Limitations and perspectives

The results of this study were obtained in a controlled environment which is not representative of daily-life conditions. Consequently, in daily-life settings, environmental disruptions, incorrect set-up, unintentional switch-off, or sensor fall might downgrade the results. Our laboratory setting reference, even though

considered a ‘gold standard’, can reach 0.02 s in timing error (Stanhope et al., 1990) and a mean accuracy of 5.3 mm for marker trajectory estimates (Chiari et al., 2005). The errors reported can, therefore, be a combination of errors of both systems. Furthermore, only configurations using sensors on the lower limbs have been tested in this study. Other configurations including those using sensors on the wrists, the chest, or the pelvis exist (Benedikt Fasel et al., 2017; Zijlstra and Hof, 2003) but were not tested as we wished to analyze the paretic and non-paretic limbs separately. Finally, we evaluated a limited number of subjects and, since CP gait patterns are very heterogeneous, a larger number of participants, especially in the CP group with a high level of disability (GMFCS II-III), would permit to strengthen the conclusions. Besides this, an increased number of participants would allow subgroup analysis within the GMFCS II-III group according to what algorithms could then be refined to be more versatile and flexible enough to fulfill the requirements of every individual clinical picture.

4.5 Conclusions

We compared three configurations of wearable sensors able to compute STP in children with CP and TD children on the base of the comparison with an optoelectronic system in the laboratory. The results showed that the configuration using sensors on both feet was more accurate for typical and regular gait patterns (i.e., for of TD children), while sensors located on the shanks and thighs performed better for moderate to severely impaired gait patterns (CP with GMFCS levels II and III). Overall, the results of this study indicate that inertial sensors proved promising for an objective evaluation of gait in daily-life. Such evaluations have the potential to shed light on patients’ daily difficulties.

Chapter 5 *

A Personalized approach to improve walking detection in real-life settings

Abstract

Although many methods have been developed to detect walking by using body-worn inertial sensors, their performances decline when gait patterns become abnormal, as seen in children with cerebral palsy (CP). The aim of this study was to evaluate if fine-tuning an existing walking bouts (WB) detection algorithm by various thresholds, customized at the individual or group level, could improve WB detection in children with CP and typical development (TD). Twenty children (10 CP, 10 TD) wore 4 inertial sensors on their lower limbs during laboratory and out-laboratory assessments. Features extracted from the gyroscope signals recorded in the laboratory were used to tune thresholds of an existing walking detection algorithm for each participant (individual-based personalization: Indiv) or for each group (population-based customization: Pop). Out-of-laboratory recordings were analyzed for WB detection with three versions of the algorithm (i.e., original fixed thresholds and adapted thresholds based on the Indiv and Pop methods), and the results were compared against video reference data. The clinical impact was assessed by quantifying the effect of WB detection error on the estimated walking speed distribution. The two customized Indiv and Pop methods both improved WB detection (higher, sensitivity, accuracy and precision), with the individual-based personalization showing the best results. Comparison of walking speed distribution obtained with the best of the two methods showed a significant difference for 8 out of 20 participants. The personalized Indiv method excluded non-walking activities that were initially wrongly interpreted as extremely slow walking with the initial method using fixed thresholds. Customized methods, particularly individual-based personalization, appear more efficient to detect WB in daily-life settings.

* Chapter published as:
Carcreff L., Paraschiv-Ionescu A., Gerber C.N., Newman C.J., Armand S. and Aminian K. "A Personalized Approach to Improve Walking Detection in Real-Life Set-tings: Application to Children with Cerebral Palsy", Sensors, 2019, vol. 19, num. 5316. doi: 10.3390/s19235316 – with permissions of all co-authors.
My contributions: Methodology, recruitement, investigation, software, data curation, visualization, formal analysis, writing – original draft, writing-review and editing

5.1 Introduction

Wearable inertial devices have gained increasing popularity in recent years to monitor physical activity and gait-related parameters in real-life settings for clinical purposes (Chen et al., 2016; Jarchi et al., 2018). Continuous and long-term assessment of gait parameters in the community (corresponding to gait 'Performance' as defined by the World Health Organization (World Health Organization, 2002)) contributes to provide clinicians a better representation of a patient's abilities in the context of every-day life (Gosselin et al., 2018). The time spent walking, number of steps per day, maximum number of consecutive steps, mean walking speed, their variability and other ambulatory related-parameters during the day constitute precious data about a patient's performance, and can inform about activity and participation (Gosselin et al., 2018). However, accurate gait assessment in real-life settings is challenging (Anisoara Paraschiv-Ionescu et al., 2019). Daily-life activities consist of a great variety of tasks, movements and body postures that are modulated in intensity and quality throughout the day, depending on a multitude of environmental and personal factors (Oberhauser et al., 2014). The detection of walking within this array of daily activities and also, the distinction between walking and non-walking types of locomotion (i.e. stair climbing and running) can prove complex.

One of the conventional methods for gait detection, i.e. walking bout (WB) detection, is based on the identification of consecutive steps, each step being identified from specific temporal gait events (Lee et al., 2015). Gait is a periodic activity consisting of successive gait cycles, formed by two (left and right) steps. By convention in clinical gait analysis, the cycle is divided in two phases: the stance phase where the foot is in contact with the ground and the swing phase where it is not. Body segments' acceleration and velocity have distinct properties during these two phases. Numerous gait recognition methods have used these specific features on accelerometer and/or gyroscope signals (Aminian et al., 2002; Hickey et al., 2017a; Muñoz-Organero et al., 2017; Pham et al., 2017). Commonly, peaks of shank angular velocity during the swing phase (Aminian et al., 2002; Salarian et al., 2004), or peaks of trunk or waist acceleration at foot contacts (Fortino et al., 2015; Anisoara Paraschiv-Ionescu et al., 2019; Zijlstra and Hof, 2003) are used to detect steps due to their simplicity (Kong et al., 2016), accuracy and repeatability (Pacini Panebianco et al., 2018). In most methods, fixed thresholds are defined for peak detection, limiting the use of the algorithm for a specific population (mostly healthy adults or elderly people with or without disability (Feldhege et al., 2015; Micó-Amigo et al., 2016; Pham et al., 2017; Salarian et al., 2004)), and in specific settings (mostly laboratory settings). Therefore, the performance of such algorithms decreases when the gait patterns are unusual such as in slow and/or impaired walking (Bertuletti et al., 2019; Fortino et al., 2015; Muñoz-Organero et al., 2017; Sanjay K. Prajapati et al., 2011) like in children with cerebral palsy (CP), and also when they are assessed in different settings (Pham et al., 2017; Sessa et al., 2015) and footwear (Anwary et al., 2018a). Adaptive thresholds throughout the assessment can also be set, giving the opportunity to adapt to the inter-steps variability within the monitoring (Fortino et al., 2015; Kheirkhahan et al., 2017; Lee et al., 2015). One disadvantage of this type of approach is that every non-gait activity presenting similar periodicity (such as horse riding or legs swinging while seated) will trigger false step detection (Anwary et al., 2018a; Sanjay K. Prajapati et al., 2011).

CP is a group of motor disorders resulting from damage of the developing brain, affecting about 1.8:1000 newborns (Sellier et al., 2016). Children with CP are characterized by heterogeneous impairments of the musculoskeletal system, with unilateral or bilateral body involvement. Only two thirds of children with CP can achieve community ambulation with or without mechanical walking aids (such as crutches, tripods or a walker), and independent walking is at the forefront of therapeutic objectives. In a previous study, we demonstrated that inertial sensors located on the shanks and thighs were able to accurately estimate gait parameters of children with CP and typical development (TD) in laboratory settings (Carcreff et al., 2018). However, WB detection was not assessed in this study since the laboratory setting enabled the precise

identification of the beginning and the end of the straight walking trials. There is thus a need to evaluate the performance of the system for WB detection in daily-life environments for this population.

Given the heterogeneity of movement impairment in CP, the algorithms for WB detection and gait analysis based on fixed-thresholds approaches might not be optimal. The expected signal features for normal gait are attenuated or distorted in some cases, resulting in poor algorithm performance (Sessa et al., 2015). Therefore, an adaptation of signal processing thresholds to the individual's movement features, or the so-called personalization, appears as a promising approach to improve algorithm's performance. Personalization can be achieved through different ways, e.g. by adding input parameters such as anthropometric data or level of activity (Sposaro and Tyson, 2009), by recognizing personal signal patterns (Oudre et al., 2018), or by having a training phase to create personalized gait model using machine learning (ML) techniques (Cola et al., 2017; Fortino et al., 2015). To the authors' knowledge, only one study tested an adaptive approach in children with CP and found acceptable accuracy using Random forest and support vector machine for walking detection (Ahmadi et al., 2018). The major drawback of pattern recognition and ML algorithms is the generalization of the model in different environments (Ahmadi et al., 2018) and populations (Oudre et al., 2018). Furthermore, ML approaches need a high amount of data to train the model and are, therefore, difficult to achieve in the context of individual personalization (Haji Ghassemi et al., 2018). Finally, no study was found emphasizing the effect of the quality of the walking detection on the distribution of a clinically meaningful parameter.

The aim of this study was therefore to evaluate if fine-tuning an existing WB detection algorithm (Salarian et al., 2004) by various thresholds customized at the individual or group level could improve WB detection in children with CP and TD. The performance of the customized algorithms was assessed in terms of successful detection of WB. The clinical impact was assessed by quantifying the effect of an improved WB detection on the estimated walking speed distribution.

We hypothesized that tuning the algorithm based on the characteristics of the individuals' movement pattern recorded in laboratory settings would improve the performance of WB detection in daily-life settings and have a significant impact on the walking speed estimation.

5.2 Materials and methods

5.2.1 Participants

Children and adolescents diagnosed with CP, and TD children were evaluated for this observational cross-sectional study. Participants were aged between 8 and 20 years. The inclusion criteria for the CP group were ability to walk in the community with or without mechanical aids, corresponding to levels of Gross Motor Function Classification System (GMFCS) I, II or III (Palisano et al., 1997). A balanced number of individuals per GMFCS levels was sought for this sample of participants in order to have a good representation of the heterogeneity in walking abilities. All participants provided written consent, and the protocol was approved by the hospital's institutional ethical committee (CCER-15-176).

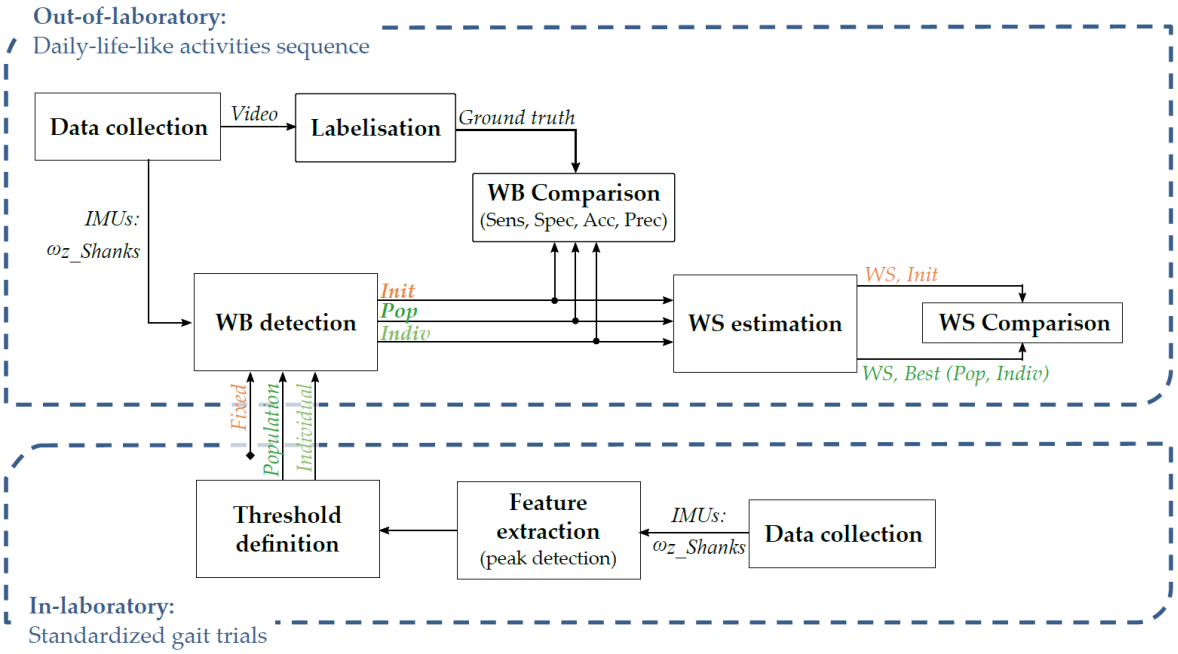
5.2.2 Protocol and material

The participants were evaluated in a single measurement session which included two parts: 1) laboratory assessments for thresholds set up, and 2) out-of-laboratory assessments for validation. During the whole measurement protocol, participants wore four synchronized inertial sensors (Physilog®4, GaitUp, Switzerland) fixed on each shank and each thigh. The sensors were safely fixed with hypoallergenic adhesive film (Opsite Flexigrid, Smith & Nephew Medical, UK). All sensors measured tri-axial acceleration and angular velocity at 100Hz (range ±8g, ± 2000°/s).

1. Laboratory: Several straight gait trials were performed by the participants on a 20m walkway, at 3 self-defined walking speeds: spontaneous, slow and fast. A total of 10 to 15 trials were recorded for each participant.
2. Out-of-laboratory: A sequence of 'daily-life-like' activities was performed in the hospital corridors and hospital surroundings including static postures of lying, sitting and standing, walking on various surfaces (stones, grass, tarmac), along straight or curved trajectories, up and down stairs, and other free activities of the participant's choice such as running, jumping or playing on swings. The sequence of activities lasted about 20 min and always started with a predefined body posture (lying on the back on a medical table). During the out-of-laboratory assessment, and for validation purpose, the evaluator was equipped with a camera (GoPro Hero+, USA) on his chest wearing a harness. The camera captured the participant during the entire sequence of daily-life-like activities.

5.2.3 Data processing

The following sections describe the data processing flow as shown in Figure 34.



Abbreviations: WB: Walking bouts; WS: Walking speed; Sens: sensitivity; Spec: specificity; Acc: accuracy; Prec: precision; ω_{z_Shank}: pitch angular velocity of shanks

Figure 34 – Data processing workflow diagram

5.2.3.1 Pre-processing

The inertial sensors and camera were manually synchronized by detecting the first lying posture on both the IMU signals and the video. Videos were labeled by the investigator using an open source software (BORIS) (Friard and Gamba, 2016). The type and timing of activities were exported in a csv file and were used as "ground truth" for WB validation. Data was processed and analyzed using Matlab R2017 software (Mathworks, USA). IMU data recorded in laboratory was cut into trials. Out-of-laboratory IMU data was recorded continuously from the first lying posture, easily recognizable on the acceleration signals (constant value of about 1g during at least 3sec), until the end of the recordings. For calibration, principal component analysis was performed on the 3-axis angular velocity signals of each shank to align the pitch (around the medio-lateral axis) angular velocity (ω_{z_Shank}) with the principal axis of movement during walking (Mcgrath et

al., 2018). A high-pass infinite-responses (IIR) filter was applied to the signals to remove noise and cancel possible drift effect (Salarian et al., 2004).

5.2.3.2 WB detection

As illustrated in Figure 34, three methods of WB detection were compared. The first, named 'Init', was the initial algorithm developed by Salarian et al. (Salarian et al., 2004) using fixed thresholds to detect each step. The other two methods used the same algorithm but with thresholds customized at the population level, i.e. CP or TD, named 'Pop', or personalized at the individual level, named 'Indiv', using individual data obtained in Laboratory. Both approaches were tested to demonstrate the significance of considering individuals' heterogeneity. The three methods are described in the following sections.

Initial algorithm (Init)

The method of Salarian et al. (Salarian et al., 2004) was chosen since it has largely been described in research for various non-pathological (adults (Salarian et al., 2004), elderly (Najafi et al., 2009; Rochat et al., 2010; Seematter-Bagnoud et al., 2011)) and patholocial populations (patients with osteoarthitis (Aminian et al., 2004), and Parkinson's disease (PD) (Salarian et al., 2013, 2004)), including studies with a large sample size (n > 800) (Rochat et al., 2010; Seematter-Bagnoud et al., 2011). Furthermore, it has recently been used in children with CP as a step counting reference in a semi-standardized setting (Anisoara Paraschiv-Ionescu et al., 2019). It thus has the potential to be used for WB detection in the population of children with and without CP.

In Salarian et al.'s algorithm, the starting point of WB detection is the gait cycles detection on left and right side, through the identification of local maximum peaks on the recorded *ωz_Shank* appearing around midswing (MS) (Salarian et al., 2004), as illustrated on Figure 35. The peaks with an amplitude higher than 50°/s (*Th1*) are candidates for marking MS. If multiple peaks within 0.5s (*Th2*) are detected, only the one with the highest amplitude is selected. If no consecutive MS of the same side are found within 1.5s (*Th3*), the WB is ended, assuming that a gait cycle is always shorter than 1.5s. A vector of MS times is then created for each side: one for the left (*MS_L*), and one for the right (*MS_R*) cycles.

Once the cycles are identified, the alternation of right and left steps is controlled in order to define a WB. Starting with the first stride, the algorithm iterated over all (i) strides on both vectors *MS_L(i)* and *MS_R(i)* and compared the times to ensure that MS alternated between right and left sides. For the first two steps, if no successive *MS_L(i)* and *MS_R(i)* are found within 3.5s (*Th4*), the WB is ended. Then, for the following steps, this threshold Th4 is adapted to the previous steps time intervals (*Th4adaptive = 1.5s + mean steps time interval so far detected in the WB*).

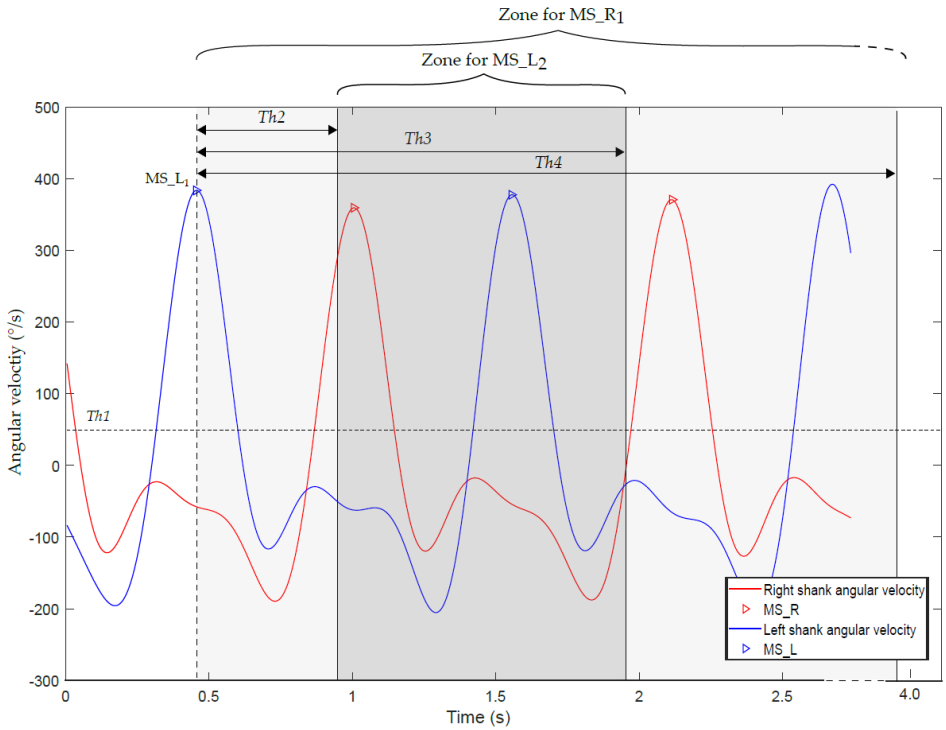
Four fixed thresholds are thus considered in Salarian et al.'s original method:

Th1 = 50°/s: Minimal amplitude of MS

Th2 = 0.5s: Minimal time between MS of the same side

Th3 = 1.5s: Maximal time between MS of the same side

Th4 = 3.5s: Maximal time between MS_R and MS_L



Two entire left cycles (in blue) and one entire right cycle (in red) are represented.
Abbreviations: MS_L: Left Midswing, MS_R: Right Midswing.

Figure 35 - Illustration of the rules used in the initial algorithm

Customized algorithms

Two customized methods were devised with the idea to tailor the four thresholds of the Init algorithm, from the gait trials obtained in laboratory for each individual (Indiv method) or each group CP or TD (Pop method). The laboratory gait trials at slow, spontaneous and fast speeds were thus used to extract the following features: minimum amplitude of MS (Th1), minimum (Th2) and maximum (Th3) time between MS of the same side, and minimum time between MS_R and MS_L (Th4) for each individual. This peak detection was made using the 'findpeak' function of Matlab on the filtered ωz_Shank and visually double-checked to ensure the accuracy and completeness of the MS detection (Figure 36).

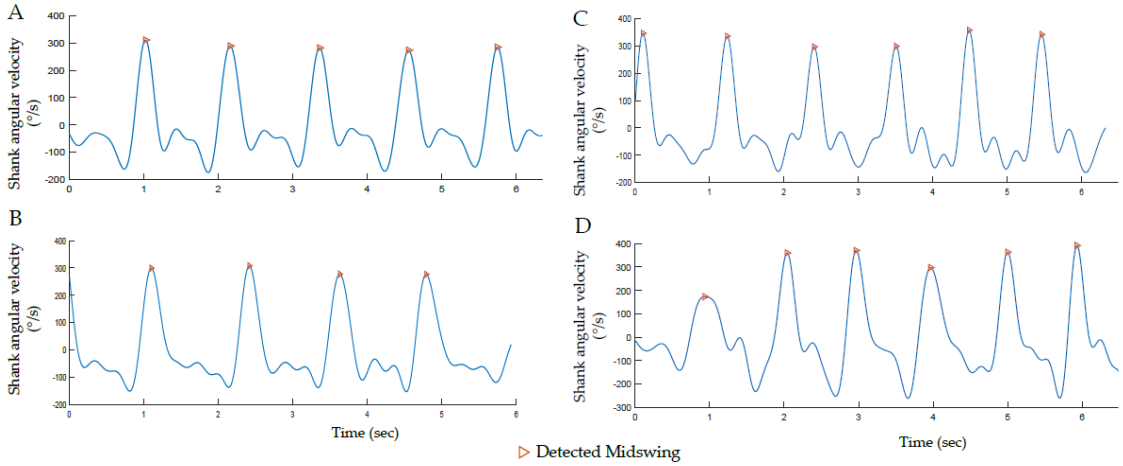


Figure 36 - Illustrative examples of Midswing detection corresponding to maximum positive peaks on the pitch shank angular velocity signal. The figure illustrates signals recorded during laboratory gait assessment in four participants with different gait patterns: (A) TD child, (B) child with CP – GMFCS I, (C) child with CP – GMFCS II and (D) child with CP – GMFCS III

Criteria used to define these new thresholds are summarized for the Indiv and Pop methods in Table 9. Pop used the signal features of the population (i.e. CP or TD) to set the new thresholds. Indiv used the signal features of each individual, and each side (left and right) independently, to account for asymmetric gait patterns in the patients with CP.

To be as inclusive as possible, and knowing that all the signal characteristics extracted corresponded to true features, the extreme values were defined as the new thresholds. So, as detailed in Table 9, the minimal values found during laboratory trials were used to define the minimal amplitude of MS (Th1) and the minimal time between MS (Th2); and the maximal values were used to define the maximal time between MS (Th3) and the maximal time between MS_R and MS_L (Th4). For Indiv, Th1 was defined as a percentage of the signal amplitude (95th percentile of ωz_Shank) since we presumed that the signal amplitude could differ between laboratory and out-of-laboratory gait. The defined thresholds were then used as inputs for the WB detection algorithm.

Table 9- Criteria for thresholds definition, based on the characteristics of the ω_{z_Shank} signal in laboratory for Pop and Indiv

Threshold	**Init**	**Pop**		**Indiv**	
		CP	**TD**	Left side	Right side
Th1 Minimal amplitude of MS (°/s)	50	Minimal MS amplitude in lab in the group	Minimal MS amplitude in lab in the group	$(\frac{\text{Minimal MS\_L amplitude in lab}}{\text{Max } \omega_{z\_shank} \text{ in lab}})$ x 95th Percentile(ω_{z_Shank}out lab)	$(\frac{\text{Minimal MS\_R amplitude in lab}}{\text{Max } \omega_{z\_shank} \text{ in lab}})$ x 95th Percentile(ω_{z_Shank}out lab)
Th2 Minimal time between MS of the same side (s)	0.50	Minimal time between MS in lab in the group	Minimal time between MS in lab in the group	Minimal time between MS_L in lab	Minimal time between MS_R in lab
Th3 Maximal time between MS of the same side (s)	1.5	Maximal time between MS in lab in the group	Maximal time between MS in lab in the group	Maximal time between MS_L max in lab	Maximal time between MS_R in lab
Th4 Maximal time between MS_R and MS_L (s)	3.5	Maximal time between MS_R and MS_L in lab in the group	Maximal time between MS_R and MS_L in lab in the group	Maximal time between MS_R and MS_L in lab	

Init: Original algorithm; Pop: Population based method; Indiv: Individual based method; MS: Midswings; MS_L: Left midswings; MS_R: Right midswings; lab: Laboratory

5.2.3.3 Walking speed computation

Walking speed was computed using the double pendulum model, introduced by Aminian et al., from the shanks' and thighs' angular velocities (Aminian et al., 2002). The WB detected with each method (i.e., Init, Pop and Indiv), and with a duration of minimum 4 steps, were analyzed with the same gait analysis algorithm (Aminian et al., 2002; Salarian et al., 2004) for walking speed estimation.

5.2.4 Analysis

Sensitivity (true positive rate), specificity (true negative rate), accuracy (true negative and positive rate) and precision (positive predictive value) were computed for each method against the video reference to evaluate their performance for WB detection. The values of these metrics vary between 0 and 1 (0 corresponding to the lowest performance and 1 corresponding to the highest performance). A tolerance of 2 seconds was applied to account for possible errors due to the manual synchronization between the sensors and camera.

The customized method (Pop or Indiv) showing the higher sensitivity, specificity, accuracy and precision for WB detection was further compared with the initial method (Init) regarding the effect on walking speed

estimation. Normality of the walking speed distributions were assessed using a Matlab open access tool (Normality test package) (Öner and Deveci Kocakoç, 2017). Results were observed on the common basic statistics describing the distribution (mean, standard deviation, median, minimum, maximum, 1st and 3rd quartiles, Skewness and Kurtosis coefficients). An appropriate inference test was used to compare the distributions of walking speed estimated for the WB detected with Init and the selected customized method. The inference test was Wilcoxon unpaired tests in case of non-normal distribution or F-tests and T-tests in case of normal distribution. The level of significance was set at 0.05. Furthermore, Cumulative Distribution Function (CDF) plots were used to illustrate the effect of the chosen customized method as compared to the initial one.

5.3 Results

5.3.1 Participants

Ten children with CP (4-GMFCS I, 3-GMFCS II, 3-GMFCS III) and 10 children with TD were included in this study. Details about their age, sex and clinical profiles are provided in Table 10.

Table 10 - Study participant details

Group (CP/TD)	**Sex**	**Age (years)** Median [IQR]	**Height (m)** Median [IQR]	**Weight (kg)** Median [IQR]	**GMFCS**	**Laterality**	**Orthosis**	**Walking aids**
TD (n=10)	7 girls - 3 boys	12.3 [11.5-13.6]	1.57 [1.52-1.62]	45.8 [40.0-56.8]	-	-	-	-
CP (n=10)	6 girls - 4 boys	13.0 [11.8-13.9]	1.56 [1.45-1.60]	43.5 [37.0-54.5]	4 GMFCS I - 3 GMFCS II - 3 GMFCS III	3 UCP - 7 BCP	6 with AFO	1 with crutches - 3 with walker*

*UCP: Unilateral CP; BCP: Bilateral CP; AFO: Ankle Foot Orthosis; * including one patient using it for long distances only; IQR: Interquartile range*

5.3.2 Laboratory gait features

For each individual, gait features related to MS were extracted from pitch angular velocity signal, ω_{z_Shank}, for straight walking performed at various speeds in laboratory setting. Mean, SD and range of these features were estimated for each CP and TD group (Table 11).

Table 11 - Population-based characteristics of the pitch angular velocity pattern extracted from laboratory gait assessments

	CP				**TD**			
Signal features	mean	SD	min	max	mean	SD	min	max
Minimal amplitude of MS (°/s)	183	65	**109**	319	270	52	**193**	354
Minimal amplitude of MS (% of signal amplitude)	58	17	29	82	76	6	66	86
Minimal time between MS (s)	0.82	0.14	**0.64**	1.10	0.87	0.12	**0.67**	1.05
Maximal time between MS (s)	1.71	0.73	1.18	**3.53**	1.41	0.21	1.11	**1.92**
Maximal time between right and left MS (s)	0.93	0.38	0.60	**1.88**	0.72	0.11	0.56	**0.99**

The values in bold were used to define the thresholds for the Pop method. Abbreviations: MS: Midswings; SD: Standard deviation

5.3.3 WB detection

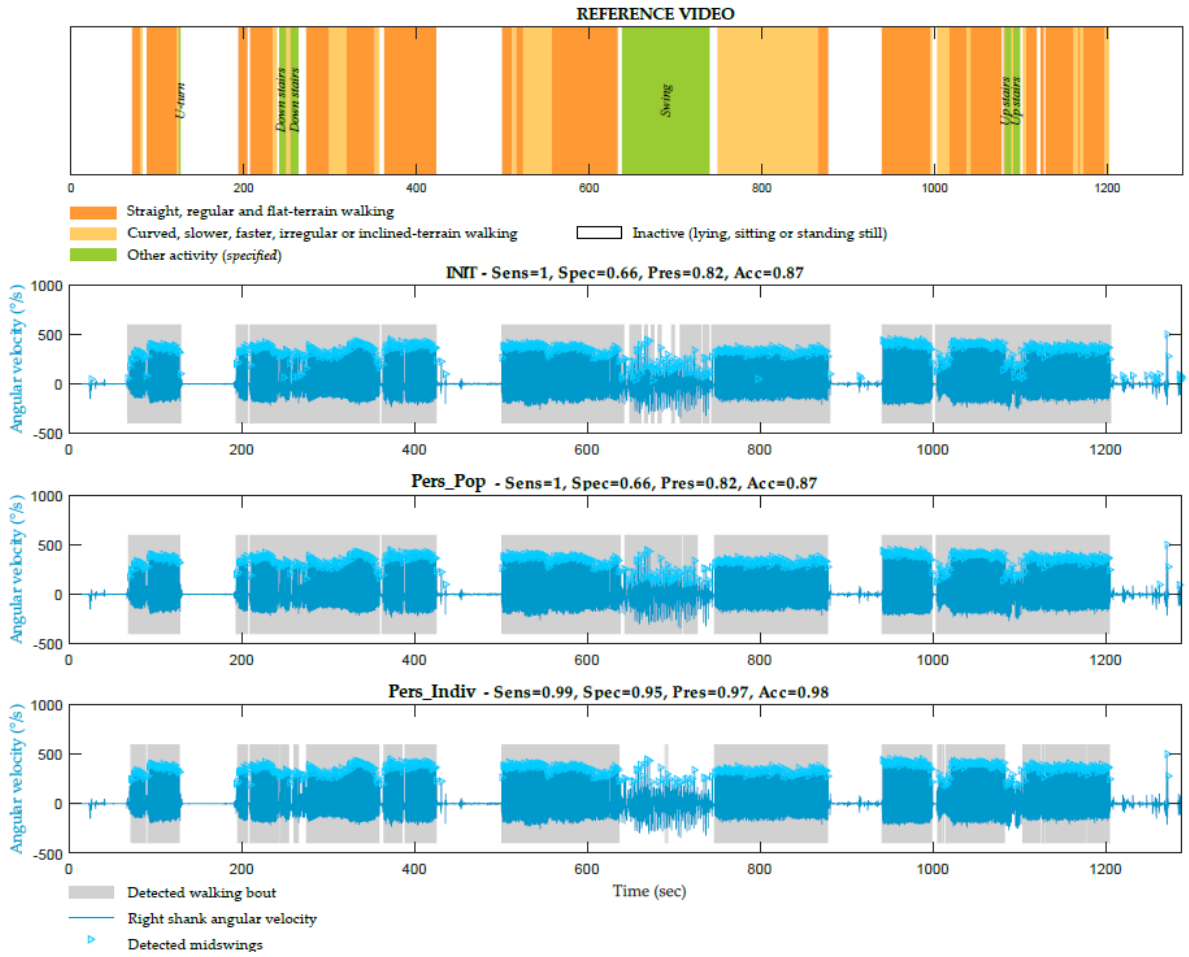
Estimated sensitivity, specificity, accuracy and precision for WB detection using each method are indicated inTable 12. The method Init had maximum sensitivity (1.00), indicating that all actual WBs were detected by the algorithm. This was also the case for the customized methods with sensitivity values of 1.00 and 0.98 for Pop and Indiv, respectively. Specificity, accuracy and precision values were lower than the sensitivity for the method Init which means that some of the detected WB did not correspond to real WB. These performance metrics increased with method Pop, and even more with the method Indiv, for both groups and for the whole study population (Table 12, next page).

Table 12 - Sensitivity, specificity, accuracy and precision of walking bouts detection for each method (based on the algorithm developed by Salarian et al. with fixed thresholds—Init, with population-based customized thresholds—Pop, and with individual-based personalized thresholds—Indiv), for each group and all the participants

	Sensitivity			Specificity			Accuracy			Precision		
	Init	Pop	Indiv	Init	Pop	Indiv	Init	Pop	Indiv	Init	Pop	Indiv
TD	1.00	1.00	0.99	0.83	0.86	0.95	0.9	0.93	0.98	0.93	0.95	0.98
(n=10)	[1.00–1.00]	[1.00–1.00]	[0.98–0.99]	[0.77–0.83]	[0.83–0.89]	[0.93–0.96]	[0.89–0.92]	[0.91–0.94]	[0.97–0.98]	[0.92–0.94]	[0.94–0.96]	[0.96–0.98]
CP	1.00	1.00	0.99	0.74	0.72	0.87	0.88	0.9	0.95	0.92	0.92	0.94
(n=10)	[1.00–1.00]	[1.00–1.00]	[0.96–0.99]	[0.67–0.82]	[0.69–0.84]	[0.83–0.90]	[0.85–0.91]	[0.88–0.92]	[0.92–0.97]	[0.88–0.93]	[0.91–0.94]	[0.93–0.96]
ALL	**1.00**	**1.00**	**0.99**	**0.79**	**0.84**	**0.91**	**0.89**	**0.92**	**0.97**	**0.92**	**0.94**	**0.96**
(n=20)	**[1.00–1.00]**	**[1.00–1.00]**	**[0.98–0.99]**	**[0.70–0.83]**	**[0.70–0.88]**	**[0.87–0.96]**	**[0.87–0.92]**	**[0.89–0.93]**	**[0.93–0.98]**	**[0.91–0.94]**	**[0.91–0.95]**	**[0.94–0.98]**

Values are presented as medians [Interquartile range].

The most important improvement was observed for specificity, indicating that Indiv, provided better results for detection of true negatives, as illustrated in Figure 37.



On the reference, orange strips correspond to straight, regular and flat-surface walking and yellow strips correspond to other type of walking such as slower, faster, on stones, on grass, on inclined-surfaces, along a curved trajectory. Green strips correspond to non-walking activities such as climbing or descending stairs, jumping, playing on the swings, running or playing around. The values of sensitivity ('sens'), specificity ('spec'), accuracy ('acc') and precision ('prec') are reported for each method. The gray strips corresponding to the detected walking bouts and the shank angular velocity signals with marks on detected midswing instants are presented superposed.

Figure 37 - Example of walking bouts detection for one patient with CP by the three methods (Init, Pop and Indiv) in comparison with the reference

In the illustrative example shown in Figure 37, the activity recorded between 650s and 750s, classified as 'other activity' on the reference video (green color), corresponded to playing on swings. The three methods detected MS during this activity because the amplitude of peaks was higher than the defined thresholds (*Th1*). However, unlike Init and Pop, the method Indiv managed to exclude most of these false positive WB, thanks to the adapted temporal thresholds between MSs.

5.3.4 Walking speed estimation

Since Indiv showed better performances for WB detection, this method was compared with the method Init regarding the walking speed distribution. The basic statistics describing the distribution are reported comparatively for the two methods and each participant in Table 13. Four illustrative examples of the

difference between the walking speed distributions are represented using CDF plots in Figure 38. We noted that with the Indiv method, for all the participants except for one child with CP, a higher number of WB was detected, with a lower number of total gait cycles throughout the whole daily-life-like activity sequence. We observed a low impact of the personalized method on mean, standard deviation, median, maximum and quartiles of walking speed (up to 0.07m/s difference overall). However, minimal walking speed changed of more than 0.4 m/s for half of the participants. We observed that the personalized method tended to bring the Skewness and Kurtosis coefficients toward 0, meaning that the distributions of speed with Indiv were more symmetric and normally tailed than with Init. Since walking speed distributions were not normally distributed, unpaired Wilcoxon tests were used to assess the significance of differences between distributions. Significant differences were found for seven participants (corresponding to 35% of our study population), four children with CP and three with TD. And for four other participants, the difference was close to the significance (p=0.06) (that being 55% of the study population).

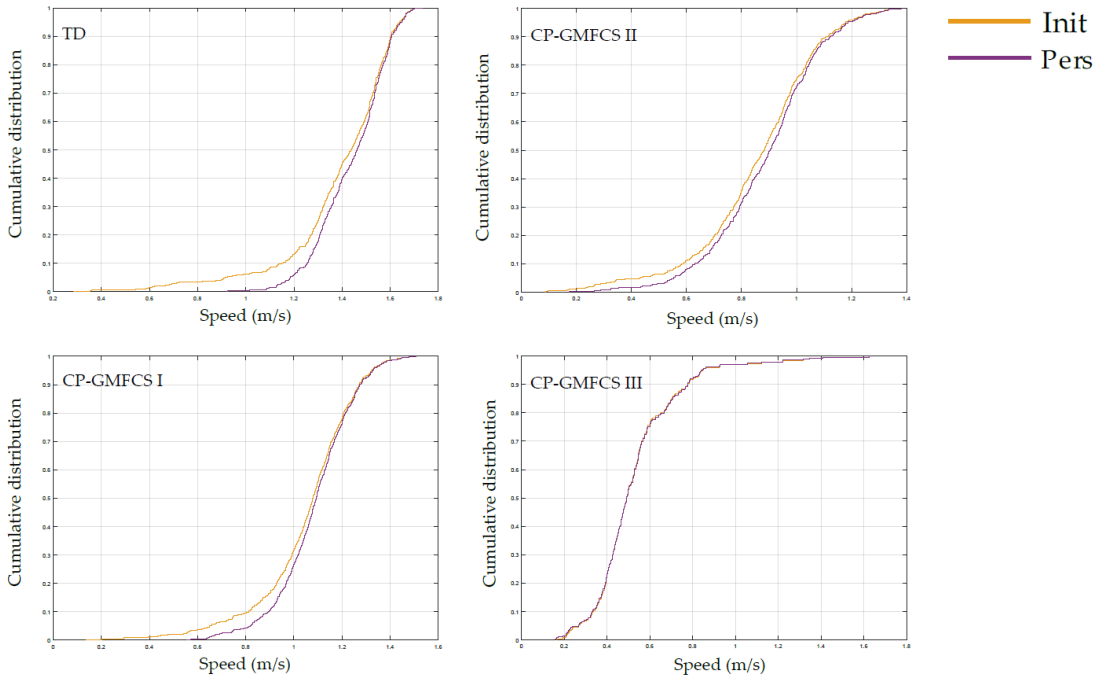


Figure 38 - CDF plots of walking speed distributions resulting from Init and Indiv walking bout detection methods for a TD child and three CP patients with different GMFCS levels

Table 13 - Walking speed distribution descriptors for methods initial and personalized

Group	GMFCS	WB (n)		Gait Cycles (n)		Mean (m/s)		SD (m/s)		Median (m/s)		Minimum (m/s)		Maximum (m/s)		1st Quartile (m/s)		3rd Quartile (m/s)		Skewness		Kurtosis		Distribution Comparison [w] (*p*-Value)
		Init	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	*Init*	*Pers*	
TD	-	10	12	571	512	1.39	1.44	0.24	0.22	1.44	1.46	0.28	0.92	1.73	1.73	1.3	1.33	1.54	1.55	−1.8	−0.5	7.37	2.82	**0.02** *
TD	-	6	13	611	553	1.19	1.22	0.23	0.21	1.23	1.24	0.23	0.64	1.67	1.67	1.09	1.12	1.32	1.33	−1.27	−0.41	6.40	3.54	0.06
TD	-	8	14	567	498	1.37	1.4	0.21	0.19	1.44	1.45	0.26	0.65	1.8	1.78	1.32	1.34	1.53	1.53	−1.81	−1.41	6.96	5.26	0.367
TD	-	7	10	589	543	1.14	1.16	0.17	0.16	1.16	1.17	0.18	0.64	1.47	1.43	1.07	1.08	1.24	1.24	−1.71	−0.34	9.64	3.48	0.31
TD	-	11	24	649	476	1.38	1.43	0.29	0.25	1.44	1.47	0.18	0.75	1.97	1.97	1.27	1.32	1.56	1.57	−1.5	−0.62	6.25	3.62	**0.041** *
TD	-	7	14	602	543	1.29	1.31	0.2	0.19	1.31	1.32	0.14	0.45	1.71	1.68	1.21	1.22	1.41	1.41	−2.02	−1.31	11.40	7.17	0.321
TD	-	7	16	541	484	1.59	1.64	0.25	0.22	1.64	1.67	0.36	0.84	2.02	2.02	1.5	1.54	1.75	1.76	−1.68	−1.01	6.93	5.08	0.067
TD	-	7	14	506	465	1.3	1.34	0.14	0.13	1.35	1.36	0.29	0.68	1.57	1.57	1.27	1.29	1.41	1.42	−2.44	−1.61	10.56	8.01	0.061
TD	-	8	9	559	517	1.32	1.33	0.16	0.16	1.35	1.35	0.11	0.35	1.64	1.64	1.26	1.27	1.42	1.43	−2.38	−1.86	12.00	9.44	0.414
TD	-	10	23	610	540	1.28	1.32	0.26	0.22	1.32	1.35	0.31	0.54	1.98	1.98	1.16	1.21	1.43	1.44	−1.14	−0.65	5.24	4.71	**0.007** *
CP	1	8	10	520	473	1.31	1.33	0.24	0.22	1.35	1.36	0.25	0.33	1.85	1.85	1.22	1.24	1.46	1.46	−1.31	−1.07	5.96	5.40	0.377
CP	1	15	25	694	606	1.05	1.09	0.22	0.2	1.08	1.09	0.14	0.55	1.51	1.51	0.97	0.99	1.18	1.19	−1.14	−0.4	5.31	3.49	**0.047** *
CP	1	9	16	562	491	1.17	1.22	0.17	0.15	1.22	1.23	0.24	0.78	1.43	1.43	1.12	1.15	1.29	1.3	−2.05	−0.74	8.56	4.03	**0.016** *
CP	1	7	18	607	532	0.9	0.93	0.25	0.22	0.9	0.92	0.16	0.58	1.57	1.5	0.78	0.81	1.02	1.04	0.09	0.612	3.99	3.28	**0.015** *
CP	2	8	23	785	749	1.08	1.1	0.27	0.25	1.11	1.12	0.33	0.33	1.56	1.56	0.97	0.99	1.23	1.24	−0.75	−0.69	3.64	3.73	0.299
CP	2	6	23	646	601	0.94	0.98	0.18	0.16	0.97	0.98	0.16	0.30	1.5	1.5	0.87	0.9	1.05	1.06	−1.19	−0.44	5.57	5.37	**0.027** *
CP	2	14	50	808	741	0.86	0.89	0.26	0.25	0.88	0.9	0.09	0.17	1.38	1.38	0.74	0.77	1.00	1.02	−0.74	−0.38	4.04	3.42	0.061
CP	3	21	20	378	347	0.53	0.53	0.18	0.19	0.49	0.49	0.17	0.16	1.63	1.63	0.41	0.41	0.59	0.59	1.82	1.73	8.69	8.44	0.991
CP	3	9	8	296	298	0.43	0.43	0.12	0.12	0.43	0.43	0.12	0.12	0.66	0.66	0.38	0.37	0.5	0.5	−0.35	−0.4	3.15	3.20	0.885
CP	3	17	18	817	783	0.66	0.68	0.1	0.11	0.68	0.68	0.14	0.37	1.00	1.00	0.63	0.63	0.74	0.74	−1.22	−0.24	5.78	3.91	0.707

*Pers: Indiv (individual-based personalized method); [w]: Unpaired Wilcoxon test for the comparison of the speed distribution between Init and Indiv. * indicate significant differences ($p < 0.05$) between methods. Gray gradient colors correspond gradually to the level of impairment of the participant. Negative and positive Skewness values mean that the distribution is skewed to the left and to the right respectively. Positive value of Kurtosis coefficient results from a tailed distribution whereas negative value corresponds to a flattened distribution.*

5.4 Discussion

This study aimed to evaluate if customized thresholds associated with methods using wearable inertial sensors can improve gait detection for children with or without CP. The main findings were that while both methods (Pop and Indiv) improved WB detection, Indiv provided best performance particularly in the detection of true negatives. Additionally, the clinical impact of such an improvement was investigated with the walking speed distribution over a 20-minutes sequence of daily-life-like activities. The results showed that the proposed individual-based personalized method had an effect on the distribution of walking speed for 35% of the participants. These findings could therefore meet clinicians since trustworthy data about the patient's performances in daily life is required for therapeutic decisions.

The fixed thresholds of the initial method used in this study were designed and validated in laboratory settings for elderly people suffering from PD (Salarian et al., 2004). Two main reasons motivated us to evaluate the potential efficiency of new, more adaptive thresholds. First, children with CP demonstrate gait patterns that are much more unusual and heterogeneous than PD patients (Armand et al., 2016) and this was shown to be a criterion for decreasing performances of WB detection algorithms based on peak identification (Bertuletti et al., 2019; Muñoz-Organero et al., 2017). The second was the assessment environment which did not represent a daily-life situation. Wearable inertial sensors are meant to be used in daily-life environments where gait variability is higher (Tamburini et al., 2018). Thus, validation of the system for the population of children with CP in out-of-laboratory settings was required.

The proposed personalized method increased the number of detected WB as compared to the initial method (Table 13) since it cuts long WB detected by the Init method into several shorter ones, excluding hesitations and turnings. Furthermore, non-walking activities were more likely to be excluded from the analysis with the individual-based personalized method since the signal pattern (amplitude and/or timing of MS) was different from those of real gait trials. While high sensitivity is decisive to detect all WBs and to quantify the daily ambulatory activity, high specificity is necessary for effective qualification of gait impairments, i.e. computing relevant gait parameters. For example, walking cadence can be the forefront parameter for an individualized intervention in a natural environment (Slaght et al., 2017). In this case, estimated cadence should effectively correspond to actual walking cadence, and not to running or stair climbing cadence, to avoid misinterpretations (Sanjay K. Prajapati et al., 2011). The customized methods allowed us to improve the specificity while keeping high sensitivity; therefore, we can conclude that the system is relevant for both, assessment of physical behavior (e.g. WB duration, distribution and frequency) and gait impairment analysis (e.g. speed, cadence, stride length). Consequently, a positive impact on the reliability of single-day physical activity and walking performance, previously reported by Gerber et al. (Gerber et al., 2019), could be expected. However, it is worth mentioning that to assess other aspect of gait such as endurance, continuous WBs including turnings and/or short breaks may be of interest. Since our proposed methods broke these WBs into many shorter WBs, gait endurance may be underestimated (Del Din et al., 2016b).

The method using thresholds customized at the population level (Pop) proved to be less specific and accurate than the personalization at the individual level (Indiv) (Table 12). This can be explained by the inter-subject variability in both groups, but especially in the group of children with CP. These results emphasized the relevance to consider not only the populations but the individuals to reach better performance of walking detection.

The distribution of computed gait parameters should be different if some false WB were excluded. This was mainly observed for the minimal walking speeds for most of participants, and actually half of them had more than 0.40m/s difference. This can have a significant impact on the interpretations since the minimal clinically important difference regarding walking speed in CP is reported to be 0.10m/s (Moreau et al., 2016).

Furthermore, we previously found that the minimal detectable changes comparing walking speed estimation during two days of daily life in children with CP and TD were less than 0.22m/s (Gerber et al., 2019), meaning that a change of 0.40m/s would have a clinical impact for a real life assessment. Unexpectedly, the customized methods were effective not only for children with CP but also for children with TD (Table 12). As far as the three patients with GMFCS III level are concerned, no significant difference was observed in walking speed distributions (Table 13), which may be explained by the fact that they chose to stay sitting on a bench during the 'free activity of their choice' because of the fatigue induced by the protocol's activities. Indeed, the participants who benefitted the most from the customization of the method were those who performed unexpected activities during the 'free activity of their choice' part of the out-of-laboratory sequence such as playing on the swings. We expect that the differences might be more important for long-term real-life measurements, since the children would perform much more of these unanticipated activities (e.g. cycling, skating, horse-riding, skiing). Additionally, the impact on other gait parameters was not tested in this study but a greater difference could be expected especially for the knee range of motion since the knees flex and extend more during swinging on the swings than during walking.

The basic idea of customization proposed in this study was to fine-tune real-life gait analysis algorithm for an individual or a group of subjects by specific gait data obtained in laboratory from the same individual or group. This approach may be applied to many other situations where wearable systems are used to analyze abnormal gait or monitor activities such as postural transitions (sit-stand, stand-sit) in real-world situations, provided that the algorithm relies on specific signal features previously characterized in the laboratory controlled situation. Actually, in many situations, patients come to clinics for diagnosis, evaluations, regular checkups and/or therapy. These visits constitute good opportunities to record a few gait trials along a straight corridor path using inertial sensors and/or other instrument such as a camera or instrumented walkway, from which personalized thresholds or parameters of interest can be defined.

Many machine learning methods have been implemented for activity recognition or gait event detection and have shown good classification accuracy in (mostly healthy) adults (Attal et al., 2015; Caldas et al., 2017). Recently, a data-driven method for foot contact events was developed in children with various pathologies, including CP, and concluded that the accuracy of their approach was sufficient for most clinical and research applications in the pediatric population (Kidzińskiid et al., 2019). Ahmadi et al. also found acceptable accuracy for walking detection in children with a low level of CP using Random forest, support vector machine, and binary decision tree classifiers (between 90.3 and 96.5% in average) (Ahmadi et al., 2018). The accuracy achieved with the customized methods was within Ahmadi et al.'s range (90% for Pop and 95% for Indiv). The advantage of the method proposed in our study, with regard to the Ahmadi et al.'s method, is its personalization at the individual basis, thus its generalization to all type of pathologies. In addition, a notable strength of the individualization of the method through individual-based thresholds is the side independency. Indeed, in a population of unilaterally affected patients, distinguishing the more and less affected sides is relevant since the gait patterns can differ (Anwary et al., 2018a).

Although in this study the amplitude and timing of MS were the only values considered from the laboratory trials to tune the customized methods, the current findings underlined the potential for further, more sophisticated adaptive algorithms. Several additional characteristics, like the shape, amplitude or frequency of the signal, could be examined to further improve the customization. The signal pattern of the whole gait cycle could be used to detect gait cycles within long term monitoring by correlation (Oudre et al., 2018). Filtering often results in attenuation of the sharpness of specific signal features (Paraschiv-Ionescu et al., 2004) so, in some cases, it can mask the information of interest. Personalized filters can improve gait event detection (Anisoara Paraschiv-Ionescu et al., 2019), especially in the CP population whose gait patterns can be noisy due to spastic movements, or drag feet (Armand et al., 2016). Moreover, the proposed approach was designed

for WB detection based on peak identification as proposed in the initial method (Salarian et al., 2004). Other methods could have been explored to adapt thresholds such as a moving window computing the root mean square (RMS) or the coefficient of variation of the signal to detect changes of signal amplitude (Kheirkhahan et al., 2017). Furthermore, a personalized approach has recently been proposed in a healthy population (30 young adults) using the signal itself to extract features (periodicity, energy, posture, etc.) to tune a step length model (online learning) (Soltani et al., 2019). This could be a relevant solution to test, to avoid the in-laboratory phase that we proposed for feature extraction. Indeed, good correlation was found between cadence and *Th2*, *Th3* and *Th4* (5.6 Supplementary information, Figure 39). Instantaneous cadence roughly estimated by a method such as Fast Fourier Transform could thus directly determine the personalized thresholds, without any prior in-laboratory phase. Further work comparing the performance of such methods with the proposed personalized method should be undertaken.

The main limitation of this study was the modest sample size and the results should be confirmed with a larger population. Regarding the method, several limitations can be mentioned. The thresholds for both customized methods were defined to be as inclusive as possible since they corresponded to the extreme values of the overall supervised gait cycles at several walking speeds. First, various percentages of these extreme values could have been tested to determine if our choice was optimal. Second, we did not evaluate the repeatability of the definition of these thresholds even though intra and inter-day variability of gait exists, especially in patients with neurological disease. A future repeatability study could emphasize the performance of our approach. Next, the amplitude of the angular velocity peaks highly depends on the sensor alignment. The principle of axis alignment using PCA relies on the assumption that the principal axis of movement is the medio-lateral axis (sagittal plane). However, in children with CP with a high level of disability (GMFCS III), frontal and transverse components can be higher than normal, which may weaken the assumption for PCA alignment. In our case, the sensors were not removed between laboratory and out-of-laboratory assessments. However, since in real life the sensors may move among days, particular attention must be paid to the axis alignment. Finally, the interpretation of ‘spontaneous’, ‘slow’ and ‘fast’ walking may differ according to the participant and can lead to limited range of speed change, in laboratory trials, necessary to threshold fine-tuning and therefore decrease the performance of WB detection in real-life measurement settings.

5.5 Conclusions

Three methods of gait detection using inertial sensors were compared; the first with fixed thresholds (Salarian et al., 2004), the second with population-based (CP-TD) thresholds, and the third with individual-based personalized thresholds. The third method was found to better improve WB detection, especially by excluding non-walking activities that were wrongly interpreted as extremely slow walking by the initial method. These findings are particularly relevant for real-life gait assessments to get a true representation of the patients’ performances. As far as the patient has the possibility to perform a quick in-laboratory or in-clinic gait measurement, the proposed approach is simple to set up, simple to implement and not specific to a pathology.

5.6 Supplementary information

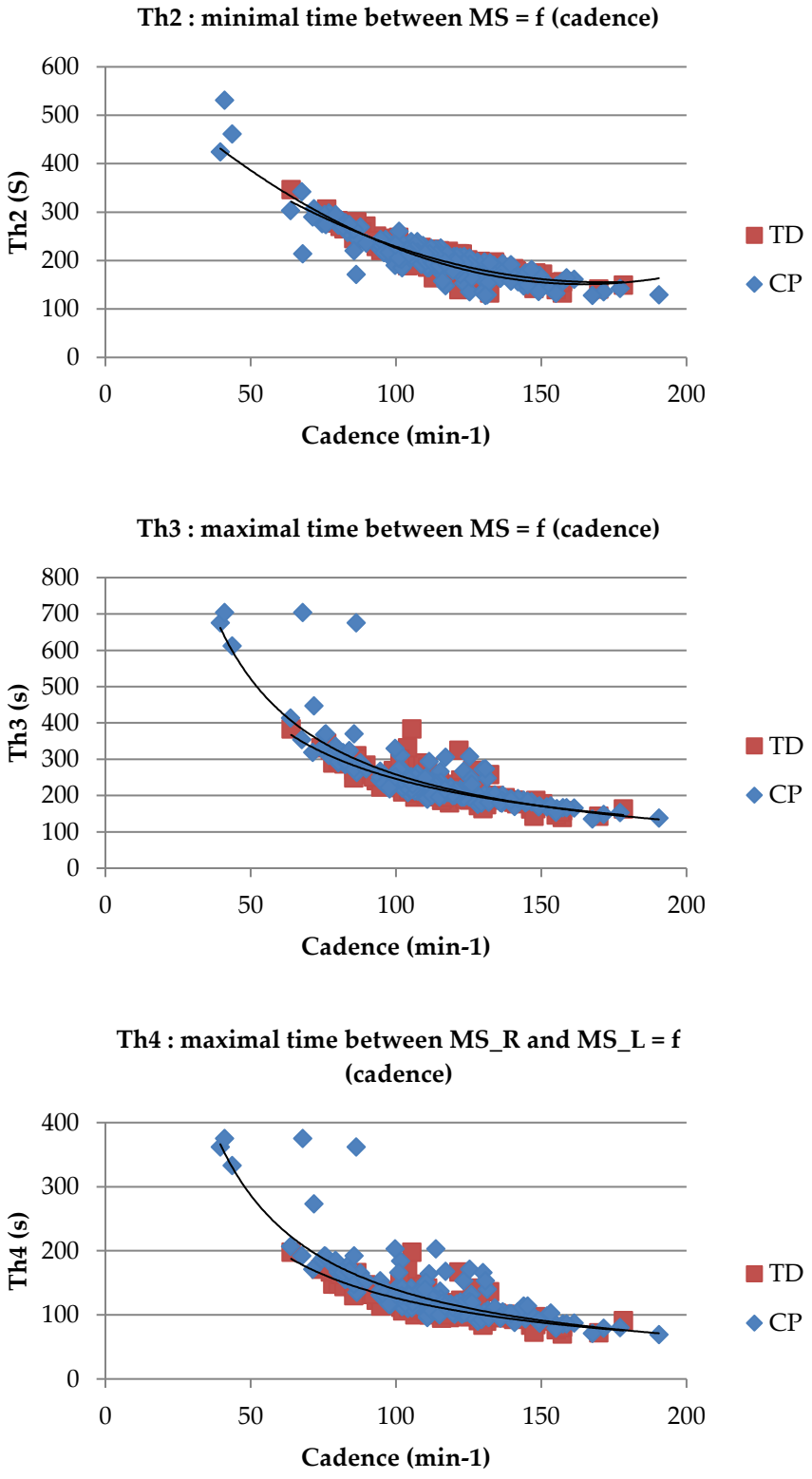


Figure 39 - Relation between the cadence of the walking bout (detected by FFT) in the laboratory and the 3 temporal thresholds Th2, Th3, Th4

Part III

CLINICAL STUDIES

This clinical part presents the three observational studies conducted to address our second specific objective which is: to compare gait parameters between standardized and unsupervised walking, in order to objectively quantify the differences between gait capacity and performance, and to examine the divergences between children with CP and children with TD. Three corresponding chapters are presented.

The first (Chapter 6) deals with the comparison between standardized gait and challenging gait under dual tasks, assessed in laboratory. The question addressed was:
How different are gait characteristics under dual tasks as compared to spontaneous walking in the laboratory?

The second (Chapter 7) presents the comparison between supervised and unsupervised gait, on the basis of a unique metric: the walking speed. The question addressed was:
To what extend spontaneous walking speed in the laboratory is representative of daily-life walking speed?
In this case, all gait episodes in real life, detected by the individual-based personalization method, were included to represent an overview of the patient's walking habits.

The third (Chapter 8) presents the comparison between supervised and unsupervised gait, focusing on multiple features of the gait function. Gait function is described by multiple gait characteristics belonging to various gait domains (pace, rhythm, variability, symmetry, amplitude, stability, smoothness and coordination) and compared between laboratory and daily life settings. The question addressed was:
Are gait characteristics assessed in daily life different from, and associated to, gait characteristics assessed in the laboratory?
Only gait episodes, detected by the individual-based personalization method, reflecting the laboratory constraint, i.e. with a travelled distance similar to the laboratory walkway length, were included in this analysis.

A direct comparison between the results in Chapter 6 and the results in Chapters 7 and 8 was not possible since different groups of children were involved. However, this is discussed in the final Chapter of this thesis (Part IV).

Chapter 6 *

Comparison between standardized gait and gait under challenging dual task conditions

Abstract

This study aimed to assess the gait and cognitive performances of children with cerebral palsy (CP) during dual tasks (DT) in comparison to typically developing (TD) children.

Method: This prospective, observational, case-control study included 18 children with CP (7 girls, 11 boys; median age 12 [10:13] years and 19 controls (9 girls, 10 boys; median age 12 [10:13y6mo] years). Performances were recorded during a simple walking task, 5 DT (walking+cognitive tasks with increasing cognitive load), and 5 simple cognitive tasks (while sitting). Gait parameters were computed using an optoelectronic system during walking tasks. Six parameters were selected for analysis by a principal component analysis. Cognitive performance was measured for each cognitive task. The dual-task cost (DTC) was calculated for each DT.

Results: Gait performance decreased in both groups as DT cognitive load increased (e.g., walking speed normalized by leg length, in simple task: 1.25 [1.15:1.46] s-1 for CP, 1.53 [1.38:1.62] s-1 for TD; DT with highest load: 0.64 [0.53:0.80] s-1 for CP, 0.95 [0.75:1.08] s-1 for TD). The CP group performed significantly worse than TD group in every task (including the simple task), but DTC were similar in both groups. A task effect was found for the majority of the gait parameters.

Interpretation: The reduced gait performance induced by DT may generate underestimated difficulties for children with CP in daily-life situations, where DT are common. This should be considered in clinical assessments.

* Chapter published as:

Carcreff L., Fluss J., Allali G., Valenza N., Aminian K., Newman C.J., Armand S.;. 2019. “The effects of dual tasks on gait in children with cerebral palsy” Gait and Posture, 2019, vol. 70, p.148-155. doi: 10.1016/j.gaitpost.2006.11.014 – with permissions of all co-authors.

My contributions: Methodology, recruitement, investigation, software, data curation, visualization, formal analysis, writing – original draft, writing-review & editing

6.1 Introduction

Cerebral palsy (CP) is the most frequent motor disability in childhood, affecting 1.8:1000 births in Europe (Sellier et al., 2016). CP affects motor control and frequently cognitive functions. Up to 65% of children with CP have executive, visuospatial, and attention deficits as well as learning disabilities (Sumnima and Jayashankar Reddy, 2013). These impairments, combined with motor limitations, can lead to increased difficulties in circumstances where cognitive and motor tasks are performed simultaneously (Schaefer, 2014), since both tasks compete for the brain's resources (Tramontano et al., 2016). While motor assessments are largely used to guide therapeutic decisions, cognitive-motor interferences are rarely taken into account.

The dual task (DT) paradigm - performing a motor task and a cognitive task simultaneously - has been widely used to study cognitive–motor interferences (Al-Yahya et al., 2011; Woollacott and Shumway-Cooke, 2002). DT protocols have been used to investigate the risk of falls among older adults (Lundin-Olsson et al., 1997) and patients with neurological disorders, such as Alzheimer's disease or multiple sclerosis (Allali et al., 2014; Maquet et al., 2010). They have rarely been studied in pediatric populations. DT assessments are appropriate to investigate the automaticity of motor control in children with and without developmental disorders (Houwink et al., 2011; Huang et al., 2003; Hung and Meredith, 2014; Manicolo et al., 2017). The underlying concept is that when a motor task is adequately learned the dedicated attentional resources are low, which allows a second task to be executed concurrently (Houwink et al., 2011). In children with CP, few studies have assessed performances during DT despite the fact that they might be relevant to understand their difficulties in daily life. Reilly et al. showed an increase of body sway in children with CP during a DT in standing, greater than in TD children (Reilly et al., 2008). Three studies concluded that a DT induces a decrease in walking speed in small samples of children with CP (≤15) (Hung and Meredith, 2014; Katz-Leurer et al., 2014; Tramontano et al., 2016). Step length, step time, and their variability changed significantly under two DT (number memorization and sound recognition) in comparison to a simple walking task (Katz-Leurer et al., 2014). The common limitations reported by the authors concerned the baseline differences between groups and the degree of cognitive demand, unadjusted to the simple task abilities of the participants (Katz-Leurer et al., 2014). The dual-task cost (DTC), which expresses change between the simple task and the DT (Kelly et al., 2010; Schaefer, 2014), is used to overcome this limitation. Considering the small sample sizes and heterogeneity of motor and cognitive tasks in previous studies, further exploration of the impact of DT in children with CP is essential. This could improve the understanding of their everyday-life difficulties (Reilly et al., 2008) leading to improvements of therapeutic strategies (Elhinidi et al., 2016).

Although walking speed is the first-line parameter to describe an individual's overall gait performance (Al-Yahya et al., 2011), it does not describe gait completely (Thingstad et al., 2015). Children with CP are also affected by problems of gait symmetry, regularity, stability, and coordination (Tugui and Antonescu, 2013), thus complementary parameters should be used to evaluate gait in this population. Pace, rhythm, asymmetry, variability, and postural control have previously been identified as five independent domains relevant for describing gait in the elderly (Lord et al., 2013) and adults with hip fracture (Thingstad et al., 2015). These domains are relevant to characterize the effects of DTs in children with CP.

This study aimed to assess the effects of DTs (using increasing cognitive loads) on gait and cognitive parameters in children with CP compared with TD controls. We hypothesized that 1) the performances of both groups would decrease under DT conditions, and 2) children with CP would experience a greater decrease due to motor and cognitive impairments resulting in higher DTCs.

6.2 Method

6.2.1 Participants

This prospective, observational, case-control study included 18 children diagnosed with CP followed in a pediatric neuro-orthopedic clinic of a tertiary hospital. Eligibility criteria were: 1) age 8–16 years old, 2) ability to walk 50 meters without mechanical walking aids (canes, tripods, walker) and/or orthoses, 3) Gross Motor Function Classification System (GMFCS) level I or II (Palisano et al., 1997), and 4) regular school curriculum. Twenty controls with equivalent ages and sex proportions, recruited via hospital employees and patients' acquaintances, were also included. Participants were excluded in cases of borderline or low intellectual ability (IQ<80) and/or behavioral symptoms which might affect participation in the protocol. No exclusion criteria were specified regarding treatments, but none of the children had surgery or botulinum toxin injections during the year prior to the assessment. Informed consent was obtained from each participant and their parents. The hospital's institutional ethics committee approved the study protocol (CCER-15-203).

6.2.2 Protocol

Each participant was evaluated once in the hospital's motion analysis laboratory. Participants were asked to walk along a straight 10-meter walkway (simple motor task: SmT) and then to repeat this while performing five successive cognitive tasks, thus creating DT. Each task was performed once to avoid any anticipation effect of the DT (Ewolds et al., 2017). After a short rest, participants were asked to sit comfortably on a chair with armrests and a backrest and to perform the same cognitive tasks in the time taken to perform that task while walking 10 meters (simple cognitive tasks: ScT). Figure 40 illustrates the experimental protocol.

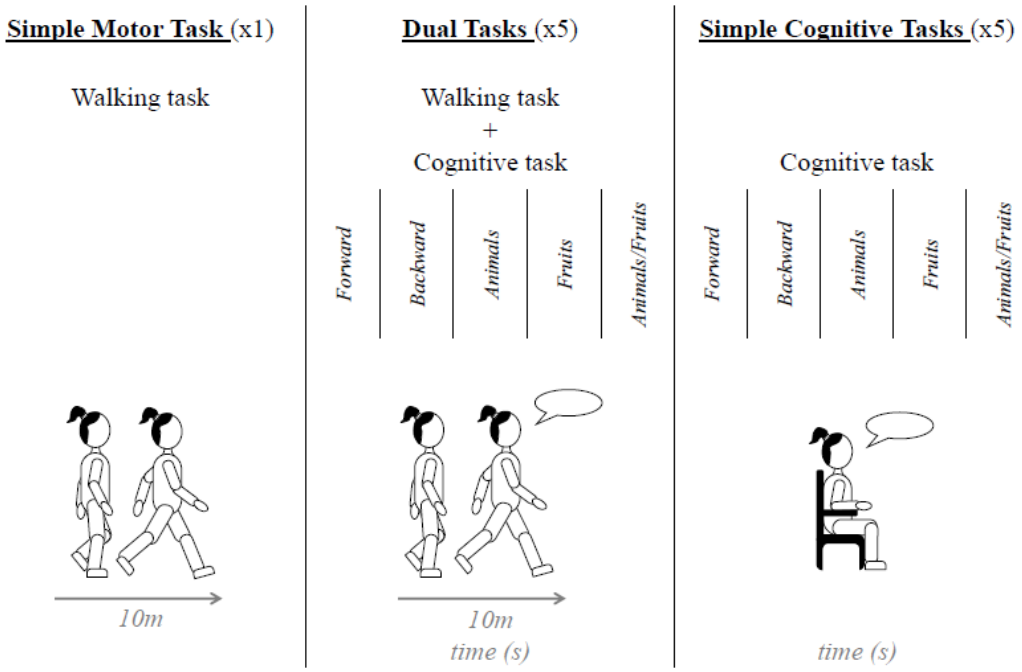


Figure 40 - Experimental protocol including the simple motor task (SmT), the dual tasks (DT), and the simple cognitive tasks (ScT)

The cognitive tasks were: counting forward from zero ('*Forward'*), counting backward from 50 ('*Backward'*), enumerating animal names ('*Animals'*), enumerating fruit names ('*Fruits'*), and alternatively enumerating animal and fruit names ('*Animals/Fruits'*). These tasks were selected as they were of short duration and could be performed orally (out loud), while walking and sitting, close to natural conditions. The tasks' level of complexity was considered to increase with the required attentional load, as follows:

Forward<*Backward*<*Animals*<*Fruits*<*Animals/Fruits*. Tasks were performed in a randomized order to avoid any fatigue effect. Before each measurement, a trained evaluator gave standard instructions. Participants were asked to perform both tasks (motor and cognitive) to the best of their ability, without prioritization.

6.2.3 Data acquisition

Participants were equipped with 16 reflective markers (14 mm diameter) placed on specific anatomical landmarks of the pelvis and the lower limbs according to the Plug-in Gait model (Davis et al., 1991). Markers' trajectories were recorded using a twelve-camera motion analysis system (Oqus7+, Qualisys, Göteborg, Sweden) at 100Hz and exported using Matlab R2012 software (Mathworks, Natick, USA) and the Biomechanical Toolkit (Barré and Armand, 2014).

6.2.4 Parameters

6.2.4.1 Gait parameters

Using the markers' trajectories, 19 gait parameters were computed, representative of 7 gait domains: rhythm, pace, variability, quality, asymmetry, stability, and coordination (Table 14). Domains were selected based on their frequent use in gait analysis and as previously described (Lord et al., 2013; Thingstad et al., 2015).
We chose to analyze the gait parameters of the most affected side for the children with CP (based on muscular strength of the lower limbs, assessed by a physiotherapist using the Medical Research Council testing), and, arbitrarily, the left side for TD children since limb symmetry was assumed (Kowalski et al., 2019).
Results were computed as means and standard deviations across the gait cycles for each walking task (each trial).
Stops and backward steps due to any hesitation were discarded. Only entire gait cycles were used for analyses.

In addition, the motor DTC (DTC_{motor}) was computed for each parameter, as described in Kelly et al. (Kelly et al., 2010):

$$DTCmotor = \frac{|\text{SmT value} - \text{DT value}|}{\text{DT value}} \text{x}100$$

Table 14 - Gait domains, gait parameters, definitions, and units

Domain	Parameter	Definition	Unit
Rhythm	Stride Time	Time between 2 successive foot strikes	s
	Stance Duration	Stance duration	% of GC [1]
	Cadence	Number of steps/min	step.min^{-1}
Pace	Stride Length	Stride length normalized by leg length	[-]
	Step Length	Step length normalized by leg length	[-]
	Walking Speed	Walking speed normalized by leg length	s-1
Variability	Gait SD	Kinematic variability based on 9 kinematic waveforms: pelvic tilt, obliquity, and rotation, hip flexion, abduction, and rotation, knee flexion, ankle dorsiflexion, and foot progression angle (Sangeux et al., 2016)	°
	Stride-Time CV [2]	Stride-time variability	%
	Stride-Length CV [2]	Stride-length variability	%
Quality	Pelvis ROM [3]	Maximum–minimum pelvic obliquity	°
	Hip ROM [3]	Maximum hip flexion–maximum hip extension	°
	Knee ROM [3]	Maximum knee flexion–maximum knee extension	°
	Ankle ROM [3]	Maximum dorsiflexion–maximum plantarflexion	°
	Gait Profile Score (GPS)	Index of overall kinematic deviation based on 9 joint angles: pelvic tilt, obliquity, and rotation, hip flexion, abduction, and rotation, knee flexion, ankle dorsiflexion, and foot progression angle (Baker et al., 2009)	°
Asymmetry	Step-Length Asymmetry Index (AI)	100*(|left step length - right step length|)/ ((left step length + right step length) * 0.5)	%
	Step-Time AI	100*(|left step time - right step time|)/ ((left step time + right step time) * 0.5)	%
Stability	Step Width	Distance between heels normalized by pelvis width at initial contact	[-]
	Heel Clearance	Maximum heel height during swing with respect to minimum during stance (Begg et al., 2007)	m
Coordination	Walk Ratio	Ratio step length/cadence (Sekiya and Nagasaki, 1998)	min.step^{-1}

[1] *GC = Gait Cycle*
[2] *CV = Coefficient of Variation*
[3] *ROM = Range Of Motion*

6.2.4.2 Cognitive scores

The cognitive score consisted of the number of correct responses counted by the evaluator (excluding repetition, omission while counting, and non-existent items) per second of the walking task. The cognitive DTC ($DTC_{cognitive}$) was computed following the same formula (Kelly et al., 2010):

$$DTCcognitive = \frac{|\text{ScT score} - \text{DT score}|}{\text{DT score}} \text{x}100$$

6.2.5 Statistical analysis

Statistical analyses were performed with RStudio software (version 1.1, Boston, USA). Non-parametric tests were performed since the normality of the distribution of gait parameters was not verified (confirmed by significant Shapiro-Wilk tests) and the sample size was small. Participant details were reported as medians [interquartile range], and gait results were presented in box plots. Participant characteristics were analyzed using Pearson Chi2 and Mann–Whitney U tests.

We used principal component analysis (PCA) (Chau, 2001) to select the gait parameters which explained the most variance within the whole population and for all the tasks. The principal components (PC) were selected so that at least 70% of variance was explained (Jolliffe and Cadima, 2016). Parameters with loading factors (i.e. correlation coefficient between variables and PC), in absolute values, greater than 0.5, were considered relevant. If more than one parameter was found to be relevant within a domain, only the parameter with the highest loading factor was selected.

Furthermore, CP and TD groups were compared using Mann–Whitney U tests. Comparisons within the groups, between tasks were assessed using Friedman ANOVA tests. The level of significance was set at 0.05. The level of significance after Bonferroni adjustments was calculated from the number of tests.

6.3 Results

6.3.1 Population description

We included 19 TD children and 18 children with CP (12 unilateral, 6 bilateral; 16 GMFCS I, 2 GMFCS II). One TD child was an extreme outlier: he often stopped with backward steps resulting from hesitations, and was excluded from the study. Table 15 shows the characteristics of the study sample. Groups were not statistically different with regards to sex (p=0.231), age (p=0.951), height (p=0.704), and weight (p=0.153).

Table 15 - General characteristics of the study sample

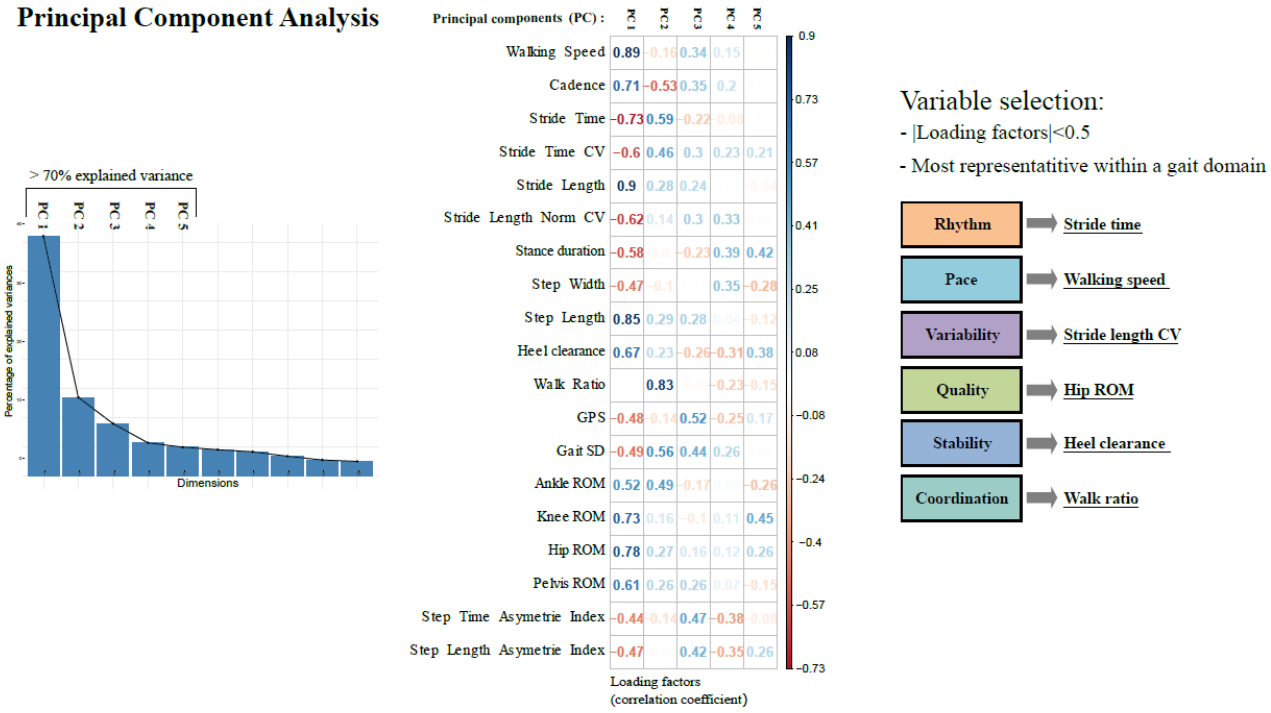
	Groups				
	TD (n=19)	CP (n=18)	p-value	95% CI	ES
Individuals characteristics					
Female (%)[k]	7 (47%)	9 (39%)	0.231	-21% to 5%	.089
Age (year)[u]	12 [10:13.5]	12 [10:13]	0.951	-2 to 2	.943
Body mass (kg)[u]	40 [31.5:47]	45 [40:57.7]	0.153	-18 to 2	.168
Body height (m)[u]	1.53 [1.41:1.64]	1.53 [1.46:1.64]	0.704	-0.13 to 0.08	.088

*[k] = values are n (%) and Pearson Khi2 test were used; [u] = values are median [interquartile range] and Mann-Whitney U test were used; *: p<0.05; ES is Cohen's effect size, 95% CI is 95% confidence interval;*

6.3.2 Variable selection

The selection of variables is illustrated in Figure 41. The first 5 PC explained 74.3% of the variance and were selected for our analysis. From these, sixteen parameters had loading factors greater than 0.5 (in absolute value). For each gait domain, the variable with the highest loading factor was selected. However, to allow comparisons with other studies, the walking speed was selected despite the fact that it had the second highest loading factor (0.89, compared to 0.90 for stride length).

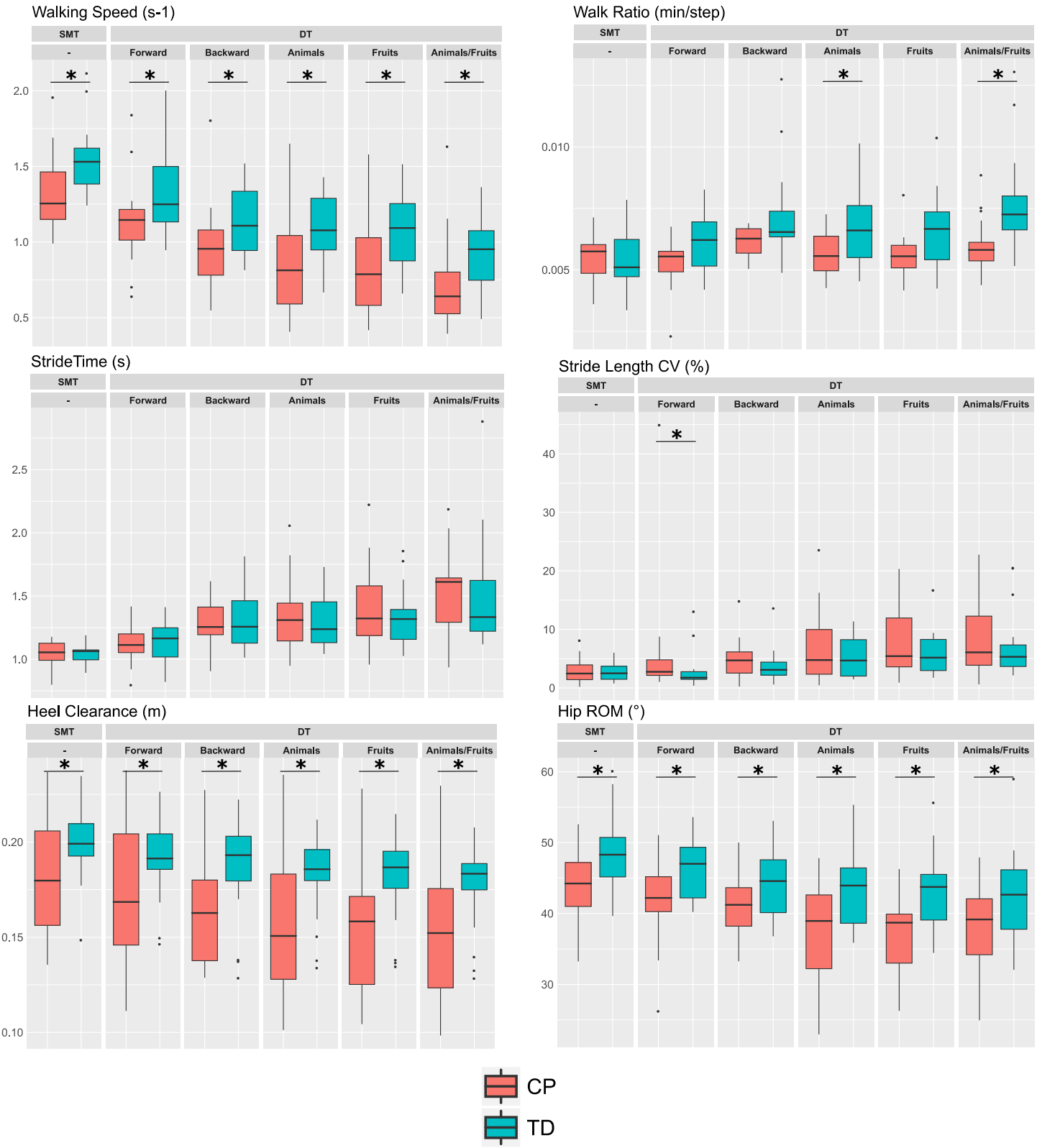
We therefore included the following six variables for analysis in our study: walking speed, walk ratio, hip range of motion (ROM), stride-length coefficient of variation (CV), stride time, and heel clearance.



On the left: variance explained by each factor in a factor analysis (scree plot); in the middle: correlation coefficients (loading factors) between the variables (rows) and the principal components (columns); on the right: variable selection based on 2 criteria.

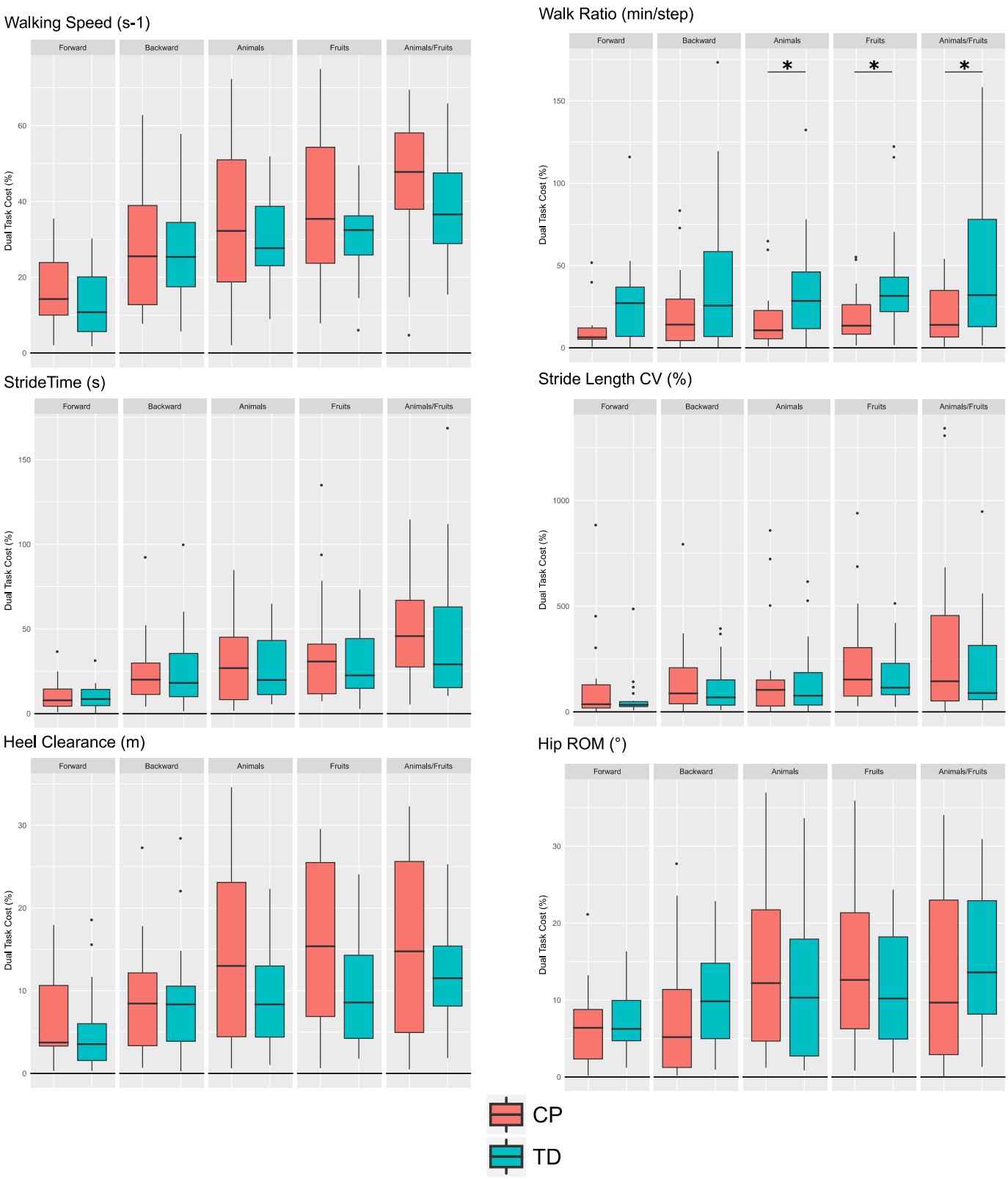
Figure 41 - Illustration of variable selection using the principal component analysis (PCA) method. Dual-task effects on the motor task

The results are presented as box plots in Figure 42. The distribution of the six selected gait parameters for each group and task was heterogeneous, particularly among children with CP. The $DTCs_{motor}$ are represented in Figure 43. Results of the comparison between the CP and TD groups (group effect) and within groups between tasks (task effect) are presented in Table 16.



** indicate significant differences (p<0.050) between groups,*

Figure 42 - Gait parameter representation for each task (vertical facets: simple cognitive task (ScT) and dual tasks (DT)) and each group (cerebral palsy (CP), typically developing (TD))



** indicate significant differences (p<0.050) between groups, assessed by Mann-Whitney U test*

Figure 43 - Dual task costs representation for each task (vertical facets: dual tasks (DT)) and each group (cerebral palsy (CP), typically developing (TD))

Table 16 - Task effect and group effect results on gait parameters and motor dual-task costs (DTC_{motor})

	Group	Simple	Forward counting	Backward counting	Animals	Fruits	Animals/ fruits	
		Group effect *p*-value between groups						**Task effect** *p*-value between tasks
Walking Speed	TD	**0.006**	**0.031**	**0.034**	**0.010**	**0.010**	**0.020**	***< 0.001***
	CP							***< 0.001***
Walk Ratio	TD	0.685	0.066	0.075	**0.029**	0.075	***0.001***	***0.014***
	CP							0.061
Stride-Length CV	TD	0.558	**0.031**	0.233	0.730	0.578	0.480	***< 0.001***
	CP							***0.014***
Hip ROM	TD	**0.017**	**0.022**	**0.039**	**0.022**	**0.011**	**0.049**	***< 0.001***
	CP							***< 0.001***
Stride Time	TD	0.574	0.915	0.845	0.620	0.518	0.438	***< 0.001***
	CP							***< 0.001***
Heel Clearance	TD	**0.034**	**0.046**	**0.029**	**0.024**	**0.007**	**0.014**	***< 0.001***
	CP							***< 0.001***
MOTOR DUAL TASK COSTS (DTC_{motor}):								
Walking Speed DTC_{motor}	TD	/	0.313	0.940	0.374	0.343	0.199	***< 0.001***
	CP							***< 0.001***
Walk Ratio DTC_{motor}	TD	/	0.066	0.258	**0.046**	**0.014**	**0.042**	0.454
	CP							0.272
Stride-Length CV DTC_{motor}	TD	/	0.730	0.671	1.000	0.578	0.584	***0.032***
	CP							**0.042**
Hip ROM DTC_{motor}	TD	/	0.538	0.098	0.480	0.358	0.855	***0.002***
	CP							***< 0.001***
Stride-Time DTC_{motor}	TD	/	0.964	1.000	0.753	0.796	0.578	***< 0.001***
	CP							***< 0.001***
Heel Clearance DTC_{motor}	TD	/	0.213	0.869	0.284	0.105	0.538	***< 0.001***
	CP							***< 0.001***

Between-group p-values were obtained using Mann–Whitney U tests; between-task p-values were obtained using Friedman ANOVA tests. Significant p-values (< 0.050) are presented in bold, and significant p-values after Bonferroni correction (< 0.001 between groups, and < 0.004 between tasks) are presented in bold and italic. CP and TD stand for cerebral palsy and typically developing, respectively.

6.3.2.1 Within-group comparisons: task effects

Decreasing gait performances were observed in both groups as the cognitive load of the tasks increased: walking speed, heel clearance, and hip ROM decreased; walk ratio, stride-length CV, and stride time increased. A significant task effect was found within both groups and for all parameters except the walk ratio in the CP group. A significant difference between tasks was also found for the DTC_{motor} except for the walk ratio DTC_{motor} in both groups.

6.3.2.2 Between-group comparisons: group effects

Children with CP walked with lower walking speed, heel clearance, and hip ROM, and higher walk ratio, stride-length CV, and stride time than the TD children. For each task, including the simple tasks, the CP and TD groups showed significant differences in walking speed, hip ROM and heel clearance. The walk-ratio was significantly different between CP and TD groups in the DT-*Animals* and *Animals/Fruits*. The stride length CV showed significant difference for the DT-*Backward*.
The CP and TD groups did not show any significant differences in their DTC_{motor} except for the walk ratio in the 3 most difficult DT (*Animals*, *Fruits*, and *Animals/Fruits*).

6.3.3 Dual-task effects on cognitive performance

6.3.3.1 Within-group comparisons: task effects

A significant task effect was found in the TD group for *Forward* and *Backward* counting (p=0.02 and 0.04, respectively): TD children enumerated more items in ScT than in DT. No task effects were found for the TD group's other tasks or for any of CP group's tasks ($p > 0.173$).

6.3.3.2 Between-group comparisons: group effects

No group effects were found for *Forward* and *Backward* tasks ($p>0.331$). A significant group effect was found in the scores for verbal fluency tasks (*Animals*, *Fruits*, and *Animals/Fruits*) in both ScT and DT: TD children enumerated more items than children with CP in those tasks. However, no significant differences between the groups were found for $DTC_{cognitive}$.

6.4 Discussion

We aimed to assess the effects of DT on the gait and cognitive parameters of children with CP. The main finding was the validation of our first hypothesis, since both populations (participants with CP and TD controls) showed decreased performances in DT conditions, although these were not statistically significant for cognitive performance. Furthermore, we demonstrated that children with CP performed worse than their TD counterparts across all tasks, including the simple task, especially for the walking speed, hip ROM and heel clearance. These results were in line with previous reports which showed a significant difference between groups in spatiotemporal parameters while walking with a concurrent task: digit memorization and sound recognition (Katz-Leurer et al., 2014) and carrying a box (Hung and Meredith, 2014). Similarly to their studies, our group of children with CP exhibited significantly worse gait performances than TD children in the simple walking task. Further analysis of the DTC_{motor} revealed that the group effect was mainly associated with the difference in the simple task, except for the walk-ratio in the verbal fluency tasks. Our second hypothesis was thus not validated, because the costs between DT and simple tasks (whether SmT or ScT) were not significantly higher in children with CP than in TD children for the majority of parameters and all the DT.
Considering that DTC is related to the recruitment of shared cortical resources for both tasks (Schaefer, 2014), our findings may in fact indicate that CP gait is not more dependent on cortical resources than TD gait during DT. Through cortical activation measures, children with CP have been shown to recruit more cortical area while walking than TD children, leading to automatization defects (Kurz et al., 2014; Sukal-Moulton et al., 2018). In literature on aging, this mechanism is known as the « dedifferentiation theory » reflecting the difficulty in recruiting specialized neural mechanisms (Heuninckx et al., 2008). We can hypothesize that, while in SmT the brain resources are not equal between the groups, in DT, both groups saturate equally their baseline resources, leading to an absence of DTC difference. Studies using fNIRS in CP population under DT might help the understanding on this topic.

Even though the DTC was not significantly different between groups, children with CP experienced greater gait difficulties when dealing with DT situations than their TD peers. For example, the median walking speed of children with CP in DT-*Backward* corresponded to the median walking speed of TD children in DT-*Animals/Fruits*. For the more complex DT, children with CP demonstrated very low gait performances. They systematically performed lower than TD children, regardless of the task or the parameter.

We observed a progressive effect of DT on gait parameters, depending on the task's cognitive load. This task effect was found for both groups, in agreement with Katz-Leurer et al. (Katz-Leurer et al., 2014) but in contrast with Hung et al. (Hung and Meredith, 2014), who did not find any task effect in the TD group. This can be related to the choice of the secondary task: carrying a box while walking being less challenging than our cognitive tasks. The task effects on DTC_{motor} revealed that cognitive tasks did not affect gait parameters equally (Friedman *p*-values below the level of significance even after Bonferroni correction), except for the walk ratio in the CP group for which no significant task effects was found.

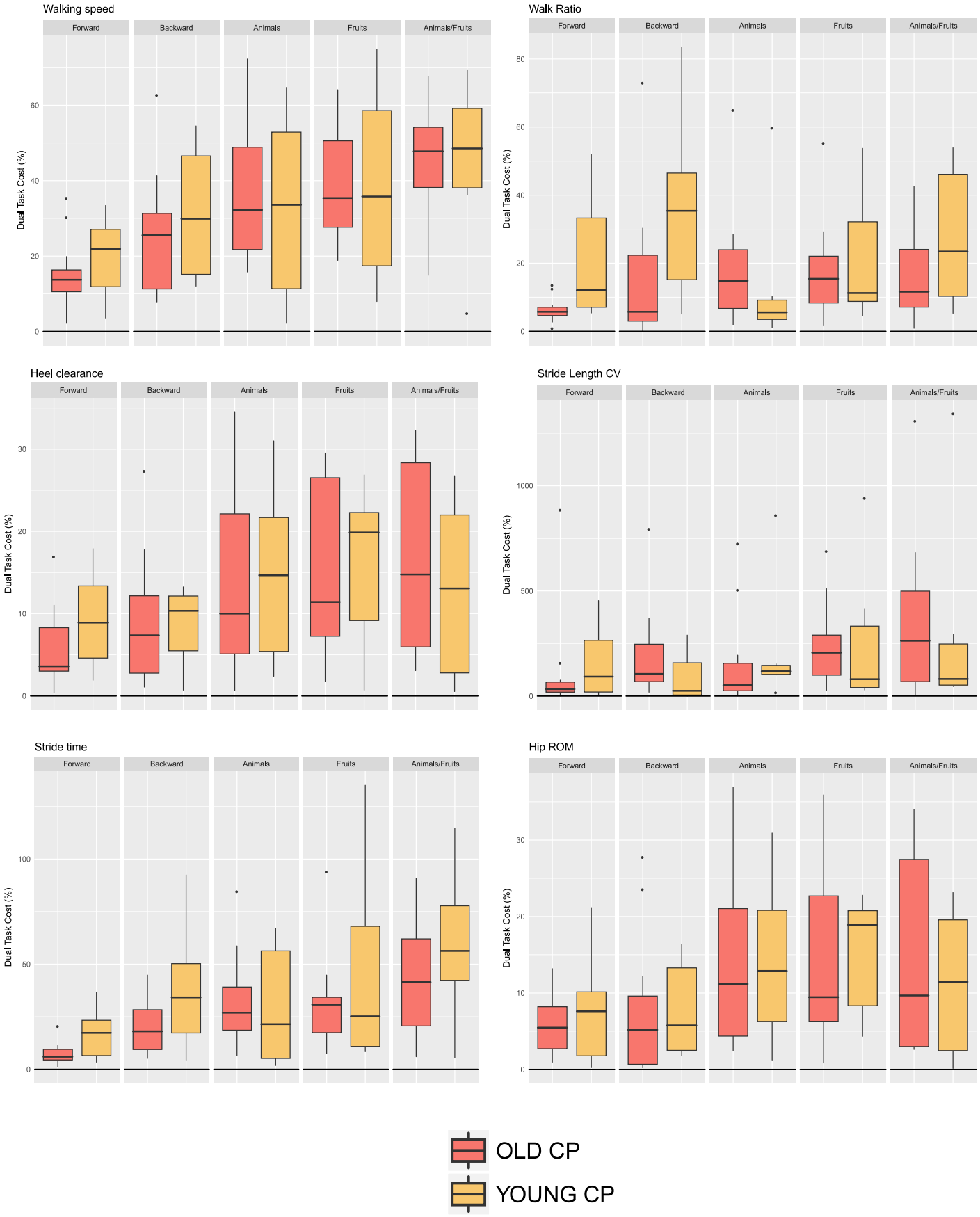
The walk ratio is the ratio between step length and cadence, which is supposed to reflect the spatiotemporal coordination of gait and be invariant in spontaneous gait (Sekiya and Nagasaki, 1998). The walk ratio of TD children increased in DT, which was mostly due to a notable decrease of their cadence whereas their stride length decreased only slightly. Among children with CP, however, both parameters decreased significantly, leading to more constant walk ratios. Although DT affected both spatial and temporal parameters in children with CP, TD children were better able to maintain their stride length.

Although the participants were asked to perform the DT without task prioritization, it appeared that they prioritized the cognitive task. Gait performances decreased, whereas cognitive scores did not change significantly from ScT to DT. This "cognitive-first" strategy, as opposed to "posture-first", has been described in studies on aging (Corp et al., 2018; Mazaheri et al., 2015) or patients with Parkinson's disease (Bloem et al., 2006), causing gait instability and falling. Although not extensively studied in children, the "cognitive-first" strategy may reflect a child-specific behavior in DT, since falling is not a major issue in comparison to older adults. We believe that this adopted strategy was also partly due to the nature of the proposed DT: the participants were constrained by the motor task (an imposed distance to walk) and had freedom in the cognitive task.

Six parameters belonging to distinct gait domains were selected on the basis of a multivariate analysis of our data. Besides the domains previously described in the literature (pace, rhythm, variability, asymmetry, and postural control), parameters relating to gait quality, such as joint angles, were added to the analysis because they provide substantial information about the gait disorders of children with CP (Armand et al., 2016), are frequently analyzed in gait analysis and were computable using our optoelectronic system. We highlighted the decrease in hip ROM and heel clearance in DT among children with CP and TD children. The present study was the first to use such an approach to assess DT effects, and we believe that it provided a more complete description of gait deviations than previous studies (Huang et al., 2003; Katz-Leurer et al., 2014). The method of parameter selection included arbitrary choices of thresholds (70% of variance explained, |loading factors|>0.5) which are debatable, but the conclusions would have been similar with other thresholds.

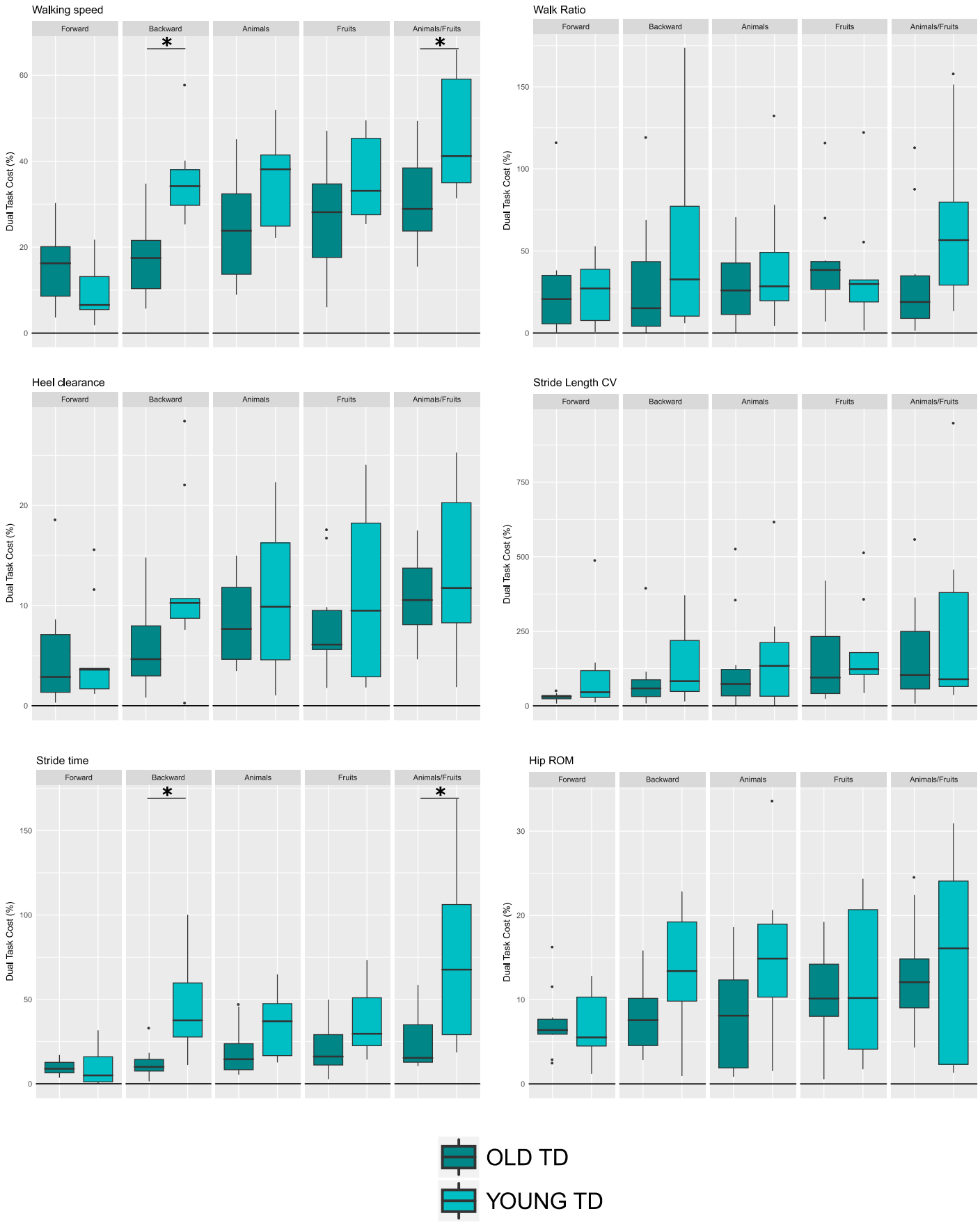
This study's main limitations were its cohort's heterogeneity. The wide age range includes an age that is a turning point regarding the maturity of gait and attentional resources, which may influence the results (Olivier et al., 2010). A complementary analysis, available in supplementary data (Figure 44 and Figure 45), supported the idea that the age heterogeneity could be one explanation for the absence of DTC difference between CP and TD groups since the youngest and oldest TD children did not show the same behavior regarding DT. Furthermore, even though this study focused on the functional impact of CP, we are aware of the heterogeneous clinical profiles between unilateral (UCP) and bilateral CP (BCP). A complementary sub-analysis, available

in supplementary data (Figure 46), comparing children with UCP and BCP did not show any differences regarding DTC, but the number of participants was insufficient within each group to draw a conclusion. Further analysis is needed to provide more specific evidence of the DT effect in the UCP and BCP populations. The power and the generalization of our analyses are limited in light of the small sample size. Another important limitation was the motion analysis system's limited capture volume, which weakens the relevance of certain gait parameters, such as the variability parameters. Additionally, assessment in laboratory settings (in underwear, walking barefoot, etc.) may not reflect real-life situations. To overcome these two last limitations, the use of wearable sensors in daily-life conditions could constitute a relevant alternative.



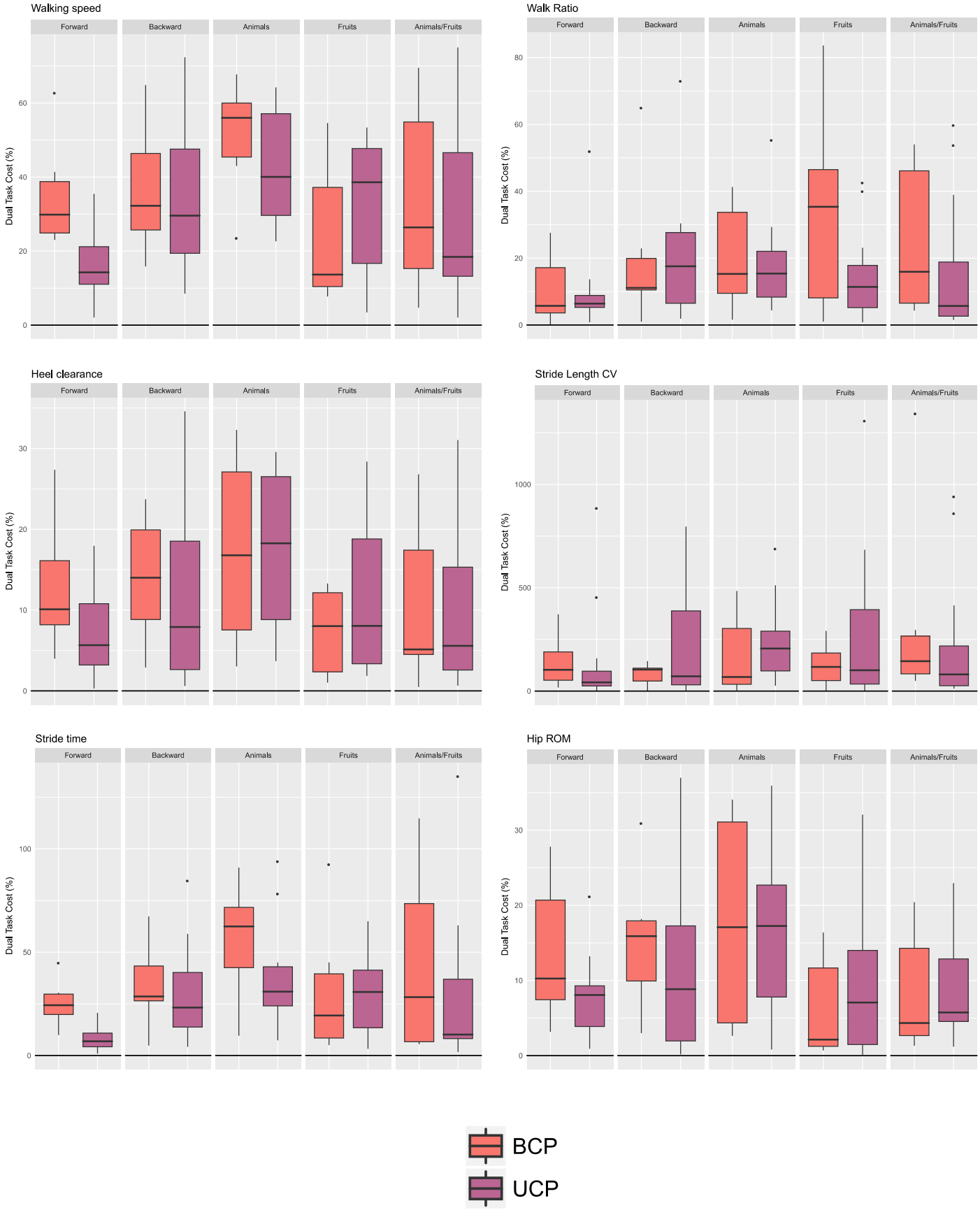
** indicate significant differences (p<0.050) between groups, assessed by Mann-Whitney U tests.*

Figure 44 - Dual task costs representation for the young and old children with cerebral palsy (CP)



** indicate significant differences (p<0.050) between groups, assessed by Mann-Whitney U tests.*

Figure 45 - Dual task costs representation for the young and old typically developing (TD) children



** indicate significant differences (p<0.050) between groups, assessed by Mann-Whitney U tests.*

Figure 46 - Dual task costs representation for the children with unilateral and bilateral cerebral palsy (UCP and BCP)

Clinical implications:

This study emphasized the importance of assessing gait in DT conditions in order to better understand limitations on the activities of children with CP. In children with mild levels of motor impairment, difficulties due to cognitive–motor interferences might be underestimated whereas they should be taken into account when devising therapeutic strategies and discussing specific adaptations at home or in school. For instance, therapists and teachers may adapt environments and instructions in such ways that they are more appropriate for a child's motor, but also cognitive abilities (Huang et al., 2003). Our study supports that training programs should integrate DT exercises (Elhinidi et al., 2016; Tramontano et al., 2016). Since daily life is not isolated from cognitive constraints, the difficulties revealed in this study are likely to influence everyday walking situations in patients' real lives.

6.5 Conclusion

Interferences between motor and cognitive tasks have significant effects on walking performance in children with and without CP. Failing to account for the effects of dual tasking in daily life may lead to an underestimation of the difficulties encountered by children with CP, including those with mild impairments. The cost of dual tasks should therefore be considered in clinical assessments and treatment planning.

Chapter 7 *

Laboratory versus daily life: the walking speed

Abstract

The purpose of this study was to compare walking speed, an important component of gait, in the laboratory and daily life, in children with cerebral palsy (CP) and with typical development (TD), and to quantify to what extent gait observed in clinical settings compares to gait in real life.

Fifteen children with CP (6 GMFCS I, 2 GMFCS II and 7 GMFCS III) and 14 with TD were included. They wore 4 synchronized inertial sensors on their shanks and thighs while walking at their spontaneous self-selected speed in the laboratory, and then during 2 week-days and 1 weekend day in their daily environment. Walking speed was computed from shank angular velocity signals using a validated algorithm. The median of the speed distributions in the laboratory and daily life were compared at the group and individual levels using Wilcoxon tests and Spearman's correlation coefficients. The corresponding percentile of daily life speed equivalent to the speed in the laboratory was computed and observed at the group level.

Daily-life walking speed was significantly lower compared to the laboratory for the CP group (0.91 [0.58-1.23] m/s vs 1.07 [0.73-1.28] m/s, p=0.015), but not for TD (1.29 [1.24-1.40] m/s vs 1.29 [1.20-1.40] m/s, p=0.715). Median speeds correlated highly in CP (p<0.001, rho=0.89), but not in TD. In children with CP, 60% of the daily life walking activity was at a lower speed than in-laboratory (corresponding percentile=60). On the contrary, almost 60% of the daily life activity of TD was at a higher speed than in-laboratory (corresponding percentile=42.5). Nevertheless, highly heterogeneous behaviors were observed within both populations and within subgroups of GMFCS level.

At the group level, children with CP tend to under-perform during natural walking as compared to walking in a clinical environment. The heterogeneous behaviors at the individual level indicate that real-life gait performance cannot be directly inferred from in-laboratory capacity. This emphasizes the importance of completing clinical gait analysis with data from daily life, to better understand the overall function of children with CP and enhance their clinical care according to their specific needs.

* Chapter submitted as:

Carcreff L., Gerber C.N., Paraschiv-Ionescu A., De Coulon G., Aminian K., Newman C.J., and Armand S. « Walking speed of children with cerebral palsy: laboratory versus daily life », to the Journal of NeuroEngineering and Rehabilitation, in December 2019

My contributions: Methodology, recruitement, investigation, software, data curation, visualization, formal analysis, writing – original draft, writing-review & editing

7.1 Introduction

The World Health Organization (WHO) has emphasized the need to consider both capacity, defined as what a person can do in a standardized environment, and performance, defined as what a person does in his/her habitual environment, to describe a person's activity (World Health Organization, 2002). Since the usual environment includes the overall societal context, performance takes external and personal factors into account, unlike capacity which focuses only on functional abilities. Walking capacity and performance can thus be interpreted as walking in clinical (laboratory) and daily life settings, respectively (Bjornson, 2019).

In children with cerebral palsy (CP), gait capacity assessments are a mainstay of clinical evaluation (Gerber et al., 2019). These children, who present lifelong motor disabilities (O'Shea, 2008), are regularly assessed in clinical settings through diverse functional tests, such as the Gross Motor Function Measure (GMFM) (Alotaibi et al., 2014) and the 6-Minute Walk Test (Enright, 2003), or through an exhaustive assessment of gait deviations by means of 3D clinical gait analysis (Armand et al., 2016; Carcreff et al., 2016b). This data on gait capacity is used to identify, quantify and understand the motor disorders, and serves as a support for the management of gait deviations (Armand et al., 2016). However, walking under the supervision of the clinician in a laboratory may not always be representative of usual walking (Gosselin et al., 2018). The patient's capacity is usually overestimated as he/she shows the best of him/herself to please the care providers (Toosizadeh et al., 2015), a phenomenon often referred to as the 'Hawthorne effect' (Berthelot et al., 2011). Additional information about the patient's unsupervised walking (i.e. daily life-based gait performance) could improve the understanding of the patient's overall gait difficulties, and hence could enhance clinical decision-making and improve medical care (Bjornson et al., 2013; Young et al., 1996).

In children with CP, gait performance is mostly assessed by self- or proxy-report questionnaires which are inherently biased by subjectivity and misrepresentation (Capio et al., 2010). Since the advent of new assessment tools like accelerometer-based pedometers, actimeters or, more generally, inertial measurement units (IMU) based activity monitors, objective data can be collected from a patient's daily activity, and direct comparisons with data measured in the laboratory can be performed.

Gait capacity and performance assessed by questionnaires are positively associated in children with CP (Van Eck et al., 2009), capacity exceeding performance (Young et al., 1996). However, this relationship is not constant in time and depends on the level of impairment (classified by the Gross Motor Function Classification System- GMFCS (Palisano et al., 1997)) (Ho et al., 2017). Indeed, Van Gorp et al. have recently shown that performance keeps developing after the ceiling of capacity is reached (Van Gorp et al., 2018). Recent studies using objective performance data have highlighted weak correlations of laboratory-based spatiotemporal and kinematic parameters with daily ambulatory activities of children with CP (Guinet and Desailly, 2017; Mitchell et al., 2015b; Nicholson et al., 2018; Wilson et al., 2015; Wittry et al., 2018). Although the comparisons were based on dissimilar metrics (i.e. Gait Deviation Index (Schwartz and Rozumalski, 2008) versus step count per day, for instance), all these findings seem to indicate that gait performance cannot be predicted directly from gait capacity (Guinet and Desailly, 2017). Using a unique metric to compare gait in the laboratory and in daily life could provide new insights into this field by quantifying the difference between both environments.

Walking speed is referred to as the sixth vital sign (Fritz and Lusardi, 2009) since it is a powerful indicator of mobility efficiency (Bjornson and Lennon, 2017; Van Ancum et al., 2019). This gait parameter constitutes the most reported outcome measure of interventions whose aim is to improve gait function (Bjornson and Lennon, 2017). It can reliably be estimated using IMUs, by direct integration, biomechanical modeling or machine learning methods (Yang and Li, 2012a). We have recently demonstrated the satisfactory accuracy and reliability of speed estimation in children with CP with low to moderate levels of motor disability (GMFCS levels I to III), using a configuration of sensors on the shanks and thighs (Carcreff et al., 2018; Gerber et al., 2019).

Recent studies have found that clinic-based speed corresponded to the highest speeds measured in daily conditions in community-dwelling older adults (Takayanagi et al., 2019; Van Ancum et al., 2019), in patients with Parkinson's disease (Del Din et al., 2016a; Toosizadeh et al., 2015) and patients with multiple sclerosis (Supratak et al., 2018). This has not been explored in CP.

The aim of this study was to compare the walking speed, global indicator of the gait function, of children with CP in daily life and in the laboratory. Our three specific research questions were: (1) Is spontaneous walking speed in the laboratory different from daily life?; (2) Is there an association between speed in the laboratory and in daily life?; (3) How much does walking speed in the laboratory represent speed in daily life?. Analyses were also performed in healthy controls with typical development (TD) since daily-life assessments of gait function are novel in this population with a need for reference data in order to draw potential conclusions (Del Din et al., 2016b). Analyses were performed at the group level, and at the individual level, to account for the heterogeneity of the CP population.

7.2 Method

7.2.1 Study design

This was a cross-sectional study.

7.2.2 Recruitment

Children with CP were recruited from the pediatric orthopedic unit of Geneva University Hospitals using the following inclusion criteria: aged between 8 and 20 years, diagnosis of CP, ability to walk in the community with or without mechanical walking aids, i.e. with a GMFCS level (Palisano et al., 1997) between I and III. A group of children with TD, homogeneous in age and sex with the CP group, were recruited among collaborators' or patients' acquaintances. Children of both groups were excluded if they had additional impairments that limited their participation in the measurements (mental age <8years, severe visual impairment, attention deficit and/or other significant behavioral issues). All participants provided written consent, and the protocol was approved by and carried out in accordance with the hospital's institutional ethical committee.

7.2.3 Protocol

A trained investigator measured anthropometric data (shank and thigh lengths) and lower limb muscle strength. The GMFM (66-item version) (Alotaibi et al., 2014) was assessed for the children with CP by a trained evaluator to score their functional capacity (from 0 to 100, 100 being the highest capacity).

Children were equipped with wearable inertial sensors and reflective markers (optoelectronic system). They were asked to walk barefoot at a natural self-selected pace (with the instruction to walk "as usual, as you walk in the street"), back and forth on a 10-meter walkway within the gait laboratory, following a standard protocol of clinical gait analysis (Baker, 2013). A total of 4 to 10 trials were recorded for each participant, depending on their capacity and fatigue.

Next, the participants were asked to wear the sensors in their daily life, for a minimum of 10 waking hours per day, during 3 consecutive days including two week-days (school days) and one weekend day. The sensors were placed at the beginning and recharged at the end of each day of measurement by a parent, a caregiver or the participant him/herself. Previously, they received a practical training by the investigator on how to handle the sensors, i.e. turning on, fixing on body segments, turning off, charging, etc. A guide was also given to support them at home. The participants were asked to complete a diary reporting their physical activities and the eventual issues encountered with the sensors.

7.2.4 Wearable sensors

Four synchronized IMU-based devices (Physilog4®, Gait Up, Switzerland) were used, one on each shank and thigh, since this configuration was demonstrated to be the most adequate lower-limb configuration to assess the walking speed in children with CP throughout GMFCS level I to III (Carcreff et al., 2018). Each device comprised a triaxial accelerometer (range ±16g) and gyroscope (range ± 1000°/s). The sampling frequency was set at 100 Hz. During the measures in the laboratory, the devices were safely fixed with a hypoallergenic adhesive film (Opsite Flexigrid, Smith & Nephew Medical, UK). During the daily life measures, the devices were fixed with a hypoallergenic double-sided hydrogel sticky (PAL stickies, PAL Technologies Ltd., UK) and protected from falling with a handmade Elastane sleeve, or under tight pants and socks.

7.2.5 Optoelectronic system

The IMUs were synchronized with a twelve-camera optoelectronic system (Oqus7+, Qualisys Göteborg, Sweden) according to the protocol described in a previous paper (Carcreff et al., 2018). In the present study, the optoelectronic system was only used to crop continuous IMUs' data into several straight gait trials.

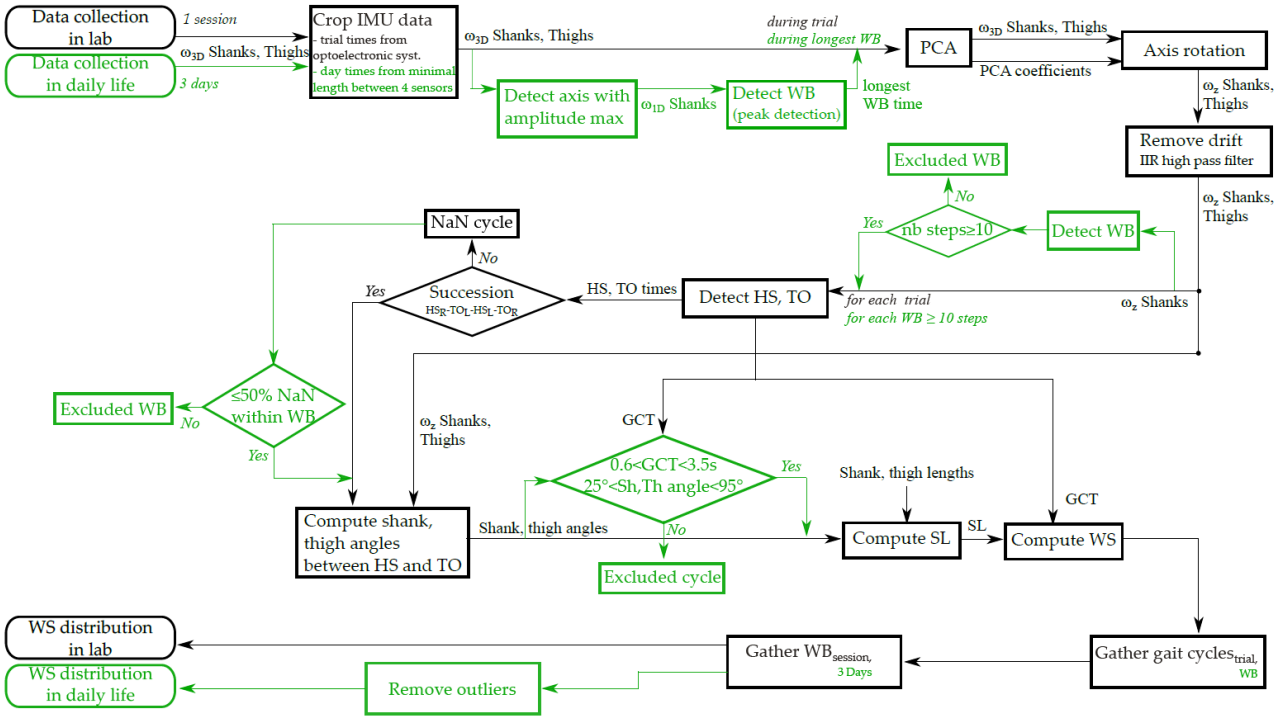
7.2.6 Data processing

Figure 47 (next page) details the data processing steps.

In-laboratory measures: The 3D continuous angular velocity data was automatically cropped into several straight walking episodes (corresponding to each back and forth trial on the walkway in the laboratory, excluding the turns) by using the optoelectronic system's start and stop of each trial. The pitch angular velocity (around the medio-lateral axis) was extracted using a principal component analysis (PCA), as the principal axis of movement during gait was assumed to correspond to the movement around the medio-lateral axis (Mcgrath et al., 2018). Gait events (heel strikes (HS), toe offs (TO)) were identified on the pitch angular velocity of the shanks as described by Aminian et al. (Aminian et al., 2002; Salarian et al., 2004). Succession of right and left steps were checked based on the times of HS and TO of each side. Shank and thigh angles for each stride were computed by trapezoidal integration between HS and TO, and between TO and HS for each walking trial with good succession of right and left steps. Walking speed was computed (cf *Walking speed computation* section) for each gait cycle of each trial.

Daily life measures: Continuous recordings of each day were cropped so that all files had the same time of recording (i.e. the minimal time shared between the 4 sensors). Walking episodes were detected using the axis of angular velocity with the highest amplitude of both shanks based on the peak detection method described by Salarian et al. (Salarian et al., 2004) personalized at the individuals level as described in a previous paper (Carcreff et al., 2019b). The 3D signal of the longest detected walking bout was used to determine the PCA coefficients to ensure selecting a steady state walking bout. Then, the axis alignment was performed on the entire signal to extract the pitch angular velocity. Drift and noise on the signal were removed using an Infinite Impulse Response (IIR) high pass filter (Salarian et al., 2004). Only the episodes with a minimum of 10 steps (5 strides) were selected for further analysis. This threshold was chosen based on inputs from clinicians and was used in previous studies (Brodie et al., 2016; Sanjay K. Prajapati et al., 2011). A minimum of ten steps also approximately corresponded to the number of steps per 10m trials in the laboratory while it would assure to have a continuous walking bout without break, less affected by the context such as short walking in a room, fidgeting, or obstacle avoidance. HS and TO were identified, the succession of right and left steps were checked, and the shank and thigh angles were computed for each stride as described in the *In-laboratory measures* section. Atypical values of gait cycle potentially related to environmental contexts (e.g., turning,

obstacle avoidance) were excluded. Criteria for exclusion were defined by taking the minimum and maximum values of each parameter from previous in-laboratory assessments at various speeds, in both the CP and the TD groups (Carcreff et al., 2019b), i.e., a gait cycle time less than 0.6s and more than 3.5s, or a shank sagittal ranges of motion less than 25° and more than 95°. This procedure was necessary to exclude the false positive detected cycles. Stride length and walking speed were estimated for each remaining gait cycles of the included walking episode.



Abbreviations: ω 1D: 1-axis angular velocity; ω3D: 3-axis angular velocity; ωz: pitch angular velocity; PCA: Principal Component Analysis; WB: Walking bout; IIR: infinite impulse response; nb steps: number of steps; HS: Heel strike; TO: Toe off; HSR: Heel strike right; HSL: Heel strike left; TOR: Toe off right; TOL: Toe off left; NaN: Not A Number; GCT: Gait Cycle Time; Sh,Th: Shank and thigh; SL: Stride length; WS: Walking speed

Figure 47 - Flow chart of data processing steps. In green are represented the steps specific to daily life measures

Walking speed computation: From in-laboratory and daily-life measurements, walking speed was computed from the pitch angular velocity of the shanks and thighs, based on the double pendulum model (Aminian et al., 2002; Salarian et al., 2004). This model uses the thigh and shank lengths and their rotation in the sagittal plane (computed by numerical integration of pitch angular velocities) between foot-strike and foot-off, to compute the right and left stride lengths. The accuracy of the system for walking speed estimation is 0.07m/s, in children with and without CP regardless of the level of impairment (Carcreff et al., 2018). Walking speed was calculated bilaterally but only the right side was considered in the overall analysis of this study, since stride parameters are theoretically identical between both sides.

7.2.7 Data analysis

7.2.7.1 Description of the ambulatory contexts

The ambulatory activities (number of steps in-laboratory, total number of steps per day in daily life, median and maximal number of consecutive steps) were described for each group and each day type (week-day or

weekend day) in order to set the context of the measurements. Cumulative Distribution Function (CDF) plots were used to visualize the speed distribution in-laboratory (CDF_{Lab}) and during each day of daily life (CDF_{DL}) on the same figure, in order to make direct visual comparisons between the distributions. CDF plots were preferred to histograms for better readability in the superposition of the distributions.

7.2.7.2 Comparisons between laboratory and daily life speeds

The results obtained from the 3 days recorded data were gathered in order to have a single daily life distribution representing both week-days and weekend days. Outlier values ($\notin$[Q1-1.5*IQR:Q3+1.5*IQR] with Q1:1st quartile; Q3:3rd quartile and IQR: interquartile range) were excluded from this single distribution (Figure 47). The level of significance for the following statistical tests was set at $p < 0.05$.

Difference between speed in laboratory and speed in daily life

Median of speed distributions in laboratory and in daily life were compared for each group (group level) and subgroups of GMFCS using the nonparametric paired Wilcoxon tests (indicated for small sample size). The speed distribution in the laboratory was also compared to the daily life distribution for each participant (individual level) using unpaired Wilcoxon tests. Effect size was computed by dividing the Wilcoxon test statistic by the square root of the number of observations, as suggested by Pallant et al. (Pallant, 2013).

Association between speed in laboratory and speed in daily life

The correlation between median speed in the laboratory and median speed in daily life was assessed by using Spearman's rank correlation coefficient (rho). Altman's guidelines were used to interpret the correlation as: poor if rho<0.2; fair if 0.21<rho<0.40; moderate if 0.41<rho<0.60; good if 0.61<rho<0.80; and very good if rho>0.81 (Altman and Altman, 1999).

Speed in the laboratory representative of speed in daily life

The percentile from the daily life distribution that corresponded to the median speed in laboratory was calculated, according to the method of Van Ancum et al. (Van Ancum et al., 2019). As an example, if the median speed in daily life equals the median speed in laboratory, the corresponding percentile would be 50.

7.3 Results

7.3.1.1 Description of the study population and the ambulatory contexts

Fifteen children with CP and 14 with TD were included in this study. The details about the CP population are provided in Table 17 and the characteristics of each group are presented in Table 18.

Table 17 - Description of the CP population

Age	Sex	GMFCS	GMFM	Topography	More affected side[1]	Walking aid in laboratory	Walking aid in DL
13.7	F	I	86.5	Uni	L		
12.3	F	I	89.7	Uni	R		
15.6	M	I	88.0	Uni	R		
20.1	M	I	88.0	Bi	R		
13.2	M	I	100.0	Bi	L		
12.3	F	I	100.0	Bi	R		
12.8	M	II	78.3	Bi	L		
10.3	F	II	65.6	Bi	R		wheelchair for long distances
9.3	F	II	67.4	Bi	L		
14	F	III	68.5	Bi	L		walker
15.8	F	III	54.1	Bi	R	walker	walker or wheelchair
8.3	M	III	57.9	Bi	R	walker	walker
11.3	M	III	54.9	Bi	L	walker	walker
11.6	F	III	63.6	Bi	L	crutches	crutches or wheelchair
17.5	F	III	37.4	Bi	R	walker	walker

[1]: based on lower limb muscle strength testing; Uni: Unilaterally affected; Bi: Bilaterally affected; R: Right; L: Left. Gray gradient colors correspond gradually to the level of impairment of the participants.

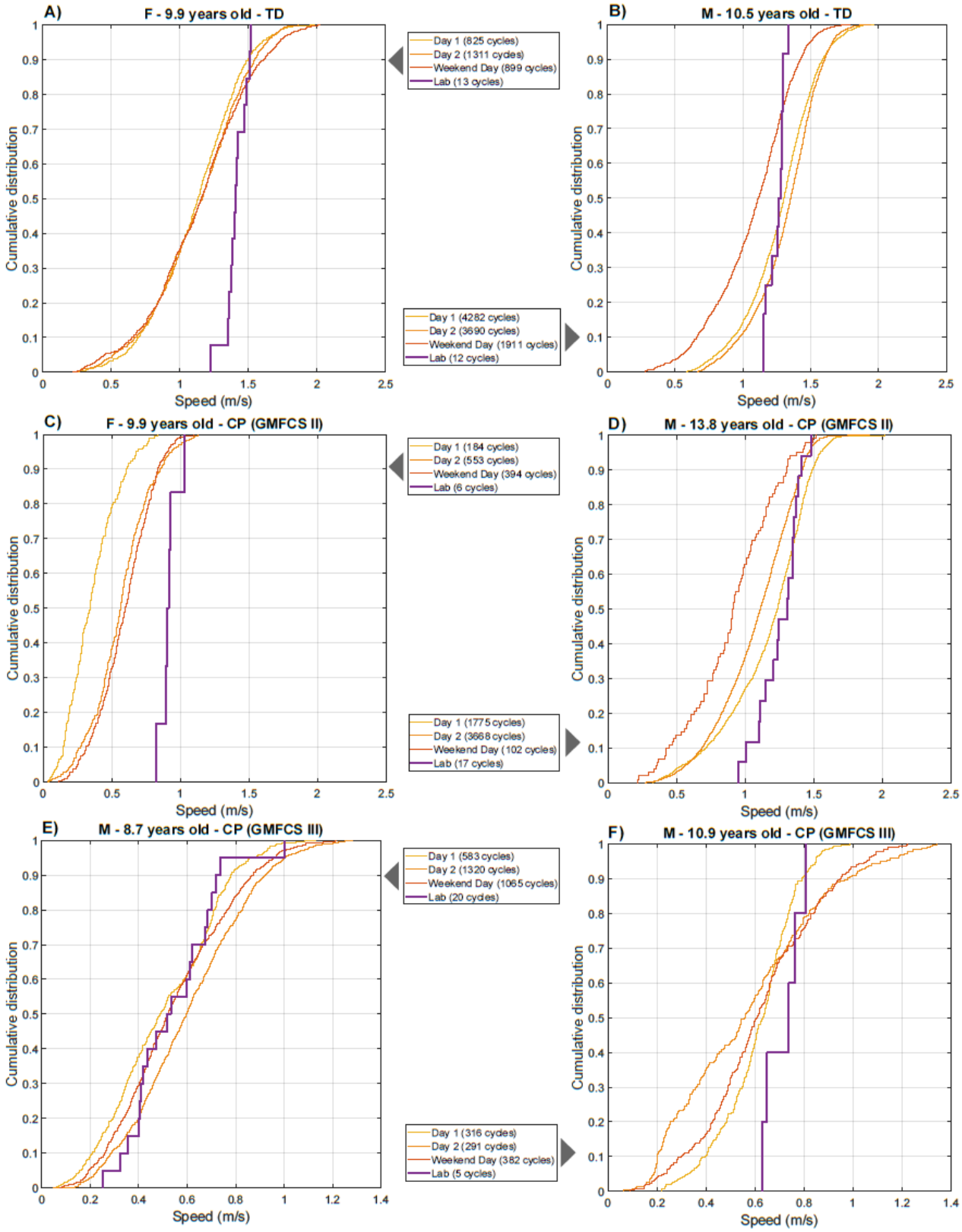
For participants with CP, the dominant clinical pattern was spastic diplegia (n=12). Therefore, the majority was affected on both sides, and half of the patients needed a walking aid for outdoor walking. The GMFM scores ranged between 37.4 and 100. One child with CP - GMFCS III did not walk enough during 2 days since she largely used her wheelchair to move, so no walking episode with more than 10 steps was detected, hence only one day (week-day) was considered for this participant. One adolescent with TD forgot to wear the sensors during the third day (weekend day). Two children with CP (GMFCS I and III) did not follow the instruction to wear the sensors on a weekend day, thus 3 week-days were assessed for them. Table 18 gives an overview of the detected ambulatory activities in each group in laboratory and daily life. In general, children with CP took fewer steps than children with TD. The number of steps taken, as well as the time spent walking during weekend days was lower compared with the week-days for both groups. Especially, the median number of consecutive steps during weekend days represented only 8% and 3% of the median number of consecutive steps during week-days in children with CP and TD, respectively. One child with TD took more than 10’000 steps and this during a week-day.

Table 18 - Groups' characteristics and detected ambulatory activity

	CP	**TD**
Group characteristics		
Sample size	15	14
Sex (n and % of girls)	9 (60%)	8 (57%)
Age (year)	12.8 [11.4:14.8]	12.2 [11.5:14.5]
Body mass (kg)	45 [36:53.5]	45.8 [37.8:57.0]
Body height (m)	1.53 [1.40:1.60]	1.57 [1.47:1.67]
Laboratory		
Number of steps	38 [28:47]	42.5 [31:46]
Daily life		
Number of steps per day [1]		
Week-days	5471 [4665:6930]	7343 [6364:9266]
Weekend days	4059 [3581:5248]	5583 [5086:6394]
Number of consecutive steps per day [1]		
Week-days	287 [136:499]	725 [532:987]
Weekend days	23 [22:25]	22 [21:26]
Maximal number of consecutive steps [1]		
Week-days	377 [154:612]	930 [744:1146]
Weekend days	143 [107:275]	376 [222:553]
Time detected walking per day (min) [1]		
Week-days	54 [24:62]	69 [58:86]
Weekend days	28 [23:32]	45 [38:58]

[1]: Considering walking bouts with a minimum of 10 steps; value are medians [IQR] per group.

The distributions of in-laboratory and daily-life speeds were visualized as superimposed CDF plots, and 6 examples are reported in Figure 48. We observed heterogeneous behaviors regarding the difference between in-laboratory and daily-life distributions. The right shift of the CDF_{Lab} in respect to the CDF_{DL} indicates that some children walked mainly at lower speeds in daily life than in laboratory (A, C and F). Others (like B, D and E) walked at similar speeds in both environments (CDFs are aligned or centered). Besides, the difference between the 3 days of daily life was not homogeneous in all participants. For instance, child A had the same speed distribution between the 3 days, whereas child B walked slower during the weekend.



Abbreviations: 'F': female, 'M': male.

Figure 48 - Six examples of speed distributions (as Cumulative Distribution Function plots) in laboratory ('Lab') and 3 days of daily life: 2 week-days ('Day 1', 'Day 2'), and 1 weekend day

7.3.1.2 Comparisons between laboratory and daily life speeds

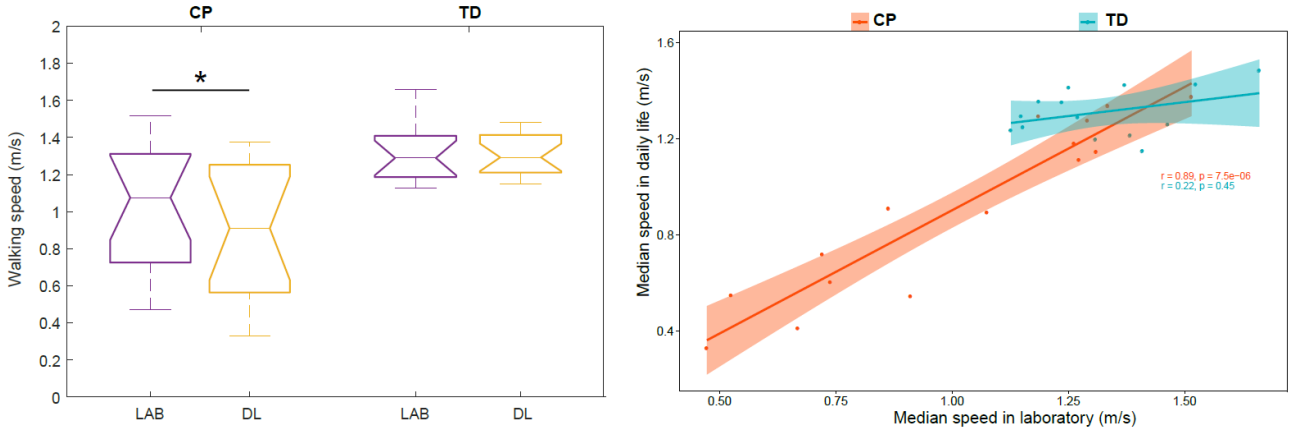
Difference between walking speed in laboratory and speed in daily life

In the CP group, the median speed in daily life (3 days assembled) was significantly lower than the median speed in laboratory (Table 19 and Figure 49 (left)). This was not the case for the TD group, for which the median speeds were similar. Furthermore, no significant difference was found when the comparison was performed for each subgroup of GMFCS (Table 19). Figure 50 illustrates the comparison between the median speed in laboratory and the distribution of daily life speeds for each participant (individual level). Proportions of individuals are summarized in Table 20. The main observations were that none of the children with CP or TD showed a median in-laboratory speed lower than the first quartile of daily life speed. Nine out of 14 (64.3%) participants with TD presented a significantly different (lower (n=4) or higher (n=5)) speed in daily life as compared to the laboratory. In the CP group, the participants who showed significantly lower speeds in daily life (n=7, 46.7%) were equally distributed among the GMFCS levels: 2 with GMFCS I, 3 with GMFCS II and 2 with GMFCS III.

Table 19 - Median speed (m/s) in the groups CP and TD in the two different measurement settings

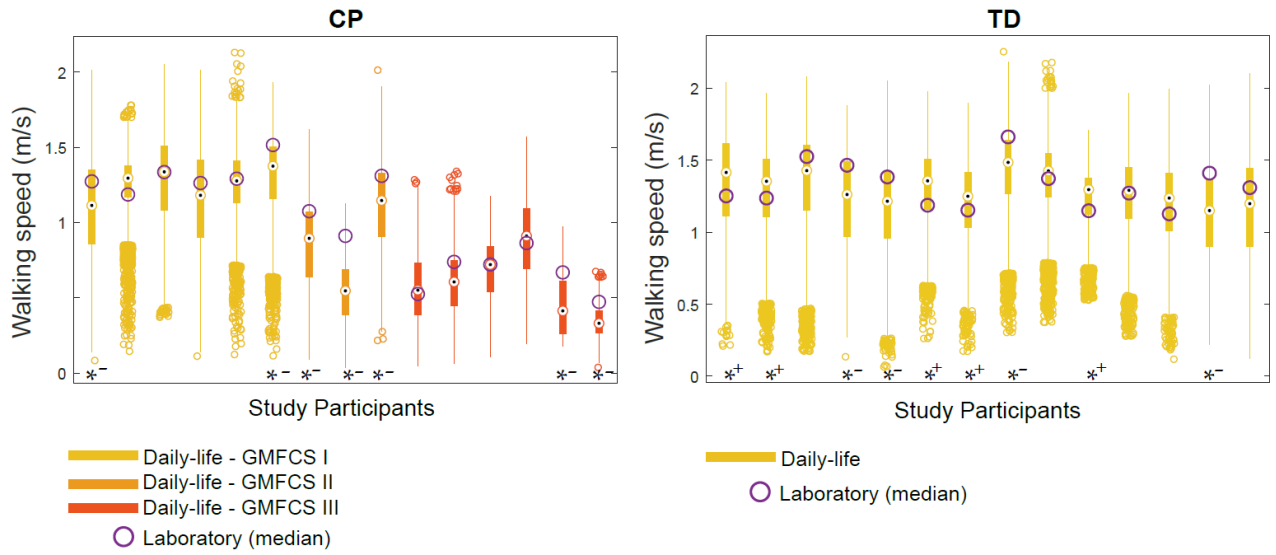
	Laboratory	**Daily life**	Comparisons [w]			Correlations [s]		Corresponding per-centile
	median [IQR]	median [IQR]	p-value	ES	95%CI	p-value	rho	median [IQR]
CP (n=15)	1.07 [0.73-1.28]	0.91 [0.58-1.23]	**0.015**	0.543	[0.02-0.16]	<**0.001**	0.89	60 [50:75]
GMFCS I (n=6)	1.28 [1.26-1.32]	1.29 [1.21-1.33]	0.313	0.141	[-0.11-0.16]	0.242	0.60	57.5 [51.3-63.8]
GMFCS II (n=3)	1.07 [0.99-1.19]	0.89 [0.72-1.02]	0.250	0.275	[0.16-0.36]	0.333	1.00	75 [75-85]
GMFCS III (n=6)	0.69 [0.56-0.73]	0.58 [0.45-0.69]	0.313	0.141	[-0.05-0.26]	**0.033**	0.89	62.5 [46.3-82.5]
TD (n=14)	1.29 [1.20-1.40]	1.29 [1.24-1.40]	0.715	0.082	[-0.10-0.10]	0.454	0.22	42.5 [35:68.75]

[W]: Paired Wilcoxon test; [S]: Spearman's rank correlation; ES: effect size; 95% CI: Confidence Interval; rho: correlation coefficient



** stands for significant difference (p<0.05). Abbreviations: 'LAB': Laboratory, 'DL': Daily life.*

Figure 49 - Comparison (left) and association (right) between median speed in the laboratory and daily life at the group level



Stars at the bottom of the box plots stand for significant difference between distributions, tested by unpaired Wilcoxon tests (⁻: Lab > Daily life; *⁺: Lab < Daily life) for each study participant.*

Figure 50 - Intra-subject comparisons between laboratory and daily life. Daily life speed distribution is represented by the box plots

Table 20 - Proportion of individuals in the categories comparing speed in laboratory and speed in daily life

	In-lab median speed < [DL speed range]	**In-lab median speed ∈ [DL speed range]**	**In-lab median speed > [DL speed range]**	**In-lab speed significantly different from DL speed (*)**
	Proportion of individuals in the group (%)			
CP (n=15)	0.0	66.7	33.3	46.7
TD (n=14)	0.0	85.7	14.3	64.3

DL: Daily life; In-lab: in-laboratory;

Association between speed in laboratory and speed in daily life

A significant very good correlation was found between the median speed in laboratory and in daily life for the CP group (rho=0.89, p<0.001) (Table 19 and Figure 49 (right)). No correlation was found for the TD group (rho=0.22, p<0.454). A very good correlation was found for the GMFCS III-subgroup only (rho=0.89, p=0.033).

Speed in laboratory representative of the speed in daily life

For the CP group, the speed in the laboratory represented the 60th percentile of the speed distribution in daily life (Table 19). Thus, the majority of children with CP walked at a lower speed during unconstrained walking. For the TD group, the corresponding percentile was 42.5, meaning that the speed in laboratory was between the 40th and the 45th percentiles of the daily life distribution of speed. Children with TD walked mostly at a higher speed during unconstrained walking. The median correspond percentile for the GMFCS-level subgroups were 57.5, 75, and 62.5 for GMFCS I, II, and III respectively.

7.4 Discussion

The aim of this study was to compare in-laboratory and daily-life walking speeds in children with CP and TD, in order to gain new insights regarding the difference between gait capacity and performance in the CP

population. Walking speed was considered to be a good indicator of the overall gait function (Middleton, A.; Fritz, S. L.; Lusardi, 2015) and knowing its distribution over 3 real-life days constituted a relevant first step to understand the difference between the global level of performance and capacity. At the group level, children with CP showed a lower walking speed in daily life as compared to the laboratory. This was not the case for children with TD. Nevertheless, at the individual level, children with CP and with TD showed highly heterogeneous behaviors, and also among the GMFCS-level subgroups. Furthermore, in contrast to controls, a high correlation was found between median speeds in laboratory and daily life for children with CP (for the whole CP group and the GMFCS III subgroup). The speed adopted by children with CP during supervised walking corresponded mostly to their higher speeds in daily life: 60% of their daily walking activity was at a lower speed than in the laboratory. On the contrary, the speed adopted by the group of children with TD during supervised walking corresponded to the lower speeds in daily life: 60% of their daily walking activity was at a higher speed than in the laboratory.

Description of the ambulatory contexts

The description of the participant's ambulatory activities showed great differences between the groups. The number of steps taken by children with CP and TD was about 5'000 and 7'000 respectively during week-days, and 4'000 and 6'000 during weekend days. This was in agreement with the results of Bjornson et al. which showed that children with TD take more steps than children with CP on a daily basis (Bjornson et al., 2007). Furthermore, this indicates that our study participants did not reach the recommendations of 10'000 to 15'000 steps per day for children and adolescents (Tudor-Locke et al., 2011), with the exception of one child with TD. Several studies have pointed out this issue, which can be explained by the current tendency of children and adolescents to be more sedentary because of screen-based activities (Wu et al., 2017). However, since the focus of the current study was not to quantify physical activity but rather to qualify walking performances within meaningful walking bouts, many short walking bouts (<10 steps) were excluded from the analysis. In natural walking, most walking bouts are short (Orendurff et al., 2008) and we most likely overestimated sedentary behaviors by the excluding short bouts.

Considerations at the group level

The results found for children with CP have important clinical implications and are not in total accordance with previous studies that used dissimilar metrics to compare gait performance with gait capacity. The slower walking speed in daily life as compared to the clinical environment was expected. It can be the result of several, and most probably, combined, reasons. Firstly, the so called 'Hawthorne effect' (doing better when observed) (Berthelot et al., 2011) may have been verified here: children with CP walked mostly faster during the clinic-based assessments. Secondly, the external factors present in the real-life environment may have played an important role in decreasing gait velocity during daily life measurements. Indeed, slowing down could reflect the difficulty when dealing with uneven surfaces and obstacles (Toosizadeh et al., 2015), decreased concentration (Brodie et al., 2016; Sanjay K. Prajapati et al., 2011), and also fatigue and cognitive-motor interferences which are two major difficulties associated with CP (Brunton and Rice, 2012; Carcreff et al., 2019a; Katz-Leurer et al., 2014). Information about the context of walking in daily life was not available as this is difficult to obtain in real-world condition unless the use of an additional system such as Global Navigation Satellite System (GNSS) (for location, indoor, outdoor) (Wang and Adamczyk, 2019) or an embedded camera (Hickey et al., 2017a). However, the use of such additional devices is problematic in our population due to their age and privacy issue. As an attempt to limit the effect of the context, only walking bouts longer than 10 steps were included. Moreover, median values as well as the whole distribution of the walking speed were considered for analysis (Wilcoxon tests, CDF plots, and corresponding percentiles). The

high correlation between in-laboratory and daily life gait speeds was unexpected. Indeed, in previous studies, only low to moderate correlations were found, implying that gait performance cannot be predicted by capacity (Gosselin et al., 2018; Guinet and Desailly, 2017; Wittry et al., 2018). Our results suggested that, for children with CP, capacity is associated to and exceeds performance (Young et al., 1996). Considering the results found in each GMFCS level, this might be especially true for the more affected children (GMFCS III). This is in contrast with the behavior of healthy controls, and probably higher functioning children with CP, for whom no correlation and no significant differences were found. This can be explained by the difference in speed ranges for children with CP and TD. Indeed, higher range of speeds in CP favored better correlation. This also meant that the capacity-performance relation can be in both directions for TD: underperforming or outperforming their capacity in daily life. This can be attributed to their ability to vary their pace depending on the context, i.e. to 'respond to unpredictability', as described by Gosselin et al. (Gosselin et al., 2018). Children with CP have less motor and attentional reserve for adaptability than their TD peers (Gosselin et al., 2018; Houwink et al., 2011), which may lead to quasi-systematic lower performances.

Recent studies which addressed this 'lab. versus free-living' clinical issue in adult and elderly populations agreed that clinic-based gait parameters were higher, and actually corresponded to the highest level of natural walking, i.e. to the 'best performance' (Brodie et al., 2017, 2016; Van Ancum et al., 2019). Even for high functioning people, the time spent walking at the level (speed or cadence) of in-laboratory walking is rare (Tudor-Locke et al., 2013). Our findings were not fully aligned with these statements. We found that walking speed in the laboratory did not systematically match with the best performance, i.e. the highest speeds in daily life. The corresponding percentile was 60 for children with CP. Children with TD did not demonstrate the same behavior as healthy older adults either, since the corresponding percentile was 42.5. This divergence of results with the adult population can be due to the more active lifestyles of children and their lower fear of falling.

This study was the first to explore the link between gait capacity and performance based on a unique and clinically-representative gait metric in children with CP. The divergence with previous results may thus be explained by the difference of outcomes. While other studies used the Gait Deviation Index to represent capacity and the daily number of steps to represent performance (Guinet and Desailly, 2017; Nicholson et al., 2018; Wilson et al., 2015), we compared the distribution of the same metric, the walking speed, in two different settings as reflections of the overall capacity and performance.

Considerations at the individual level

The results described at the group level need to be interpreted with caution since heterogeneous behaviors were found for individuals with CP, as well as those with TD, nuancing the previously mentioned group results. We found that only 46.7% of children with CP had a significant difference between supervised and unsupervised walking speed, while at the group level, the median speeds were highly significantly different. This is likely due to the small sample size and the high inter-subject variability. Indeed, the corresponding percentile ranged between 25 and 95, picturing completely different inter-subject behaviors. For children with TD, 64.3% did not follow the group results and the corresponding percentile ranged between 25 and 80. These intra-group heterogeneities are most likely due to dissimilar day-to-day lifestyles and dissimilar demonstrations of the spontaneous in-laboratory gait. Indeed, children's daily activities are very variable. Depending on the school program, physical activities differ highly between days. Also, external factors, such as the weather, were inherently not controlled during the unsupervised assessments. The protocol should have included more days of measurement, as suggested by Ischikawa et al. (Ishikawa et al., 2013) (a minimum of 6 days for the higher functioning children, and 4 days for the most affected children), to obtain more stable measures of habitual ambulatory activity. A compromise had to be found though, to decrease the risk of patients' refusing to wear

the sensors in their daily environment, as encountered for three children of our cohort. Moreover, family situations, geographic location, and the physical activity habits vary significantly across participants. All these factors could have contributed to the heterogeneity of the results. In addition, the in-laboratory behaviors may differ among children. First, although we used modified verbal commands (Nascimento et al., 2012) to instruct for 'spontaneous' speed ("walk as usual, as you were in the street"), the understanding of the instruction may have differed. A demonstration or a systematic training phase to let the participant find his spontaneous speed could have been considered (Nascimento et al., 2012). Second, the Hawthorne effect may have resulted in two different outcomes: walking faster or improving the gait pattern quality to the detriment of walking speed.
It should be noted that the heterogeneity within the CP group was not the result of the heterogeneous levels of impairments, since different results were found for the same gross motor function (GMFCS and GMFM) levels (Figure 50). This was in line with previous questionnaire-based results showing that for the same levels of capacity, different performances were observed (Holsbeeke et al., 2009). Accounting for the described individual heterogeneity, this study brought new insights, based on objective assessments, into the relevance of assessing both capacity and performance. Even if for the group with CP performance was highly associated with laboratory-based walking, the exact level of an individual's performance cannot be estimated from the laboratory.

Clinical implications

Nowadays almost all lab-based performance measures such as standardized tests, including 3D gait analysis, serve clinical-decision making, when real-life outcomes are actually the most important for the children and their families. The extent to what gait characteristics measured during 3D gait analysis correlates with unconstrained daily-life walking is still unknown (Supratak et al., 2018). It is fundamental to fill this gap in order to appreciate the meaningfulness of the clinic-based measures for the patient (Supratak et al., 2018). This study has the merit to address this issue thanks to the walking speed, a clinically meaningful parameter considered as the sixth vital sign (Fritz and Lusardi, 2009), in opposition to arbitrarily defined levels of physical activity through 'activity counts'.
This study emphasized that ecological assessments of gait should be considered in clinical routine, as a complement to in-laboratory 3D gait analysis, to obtain realistic information about motor performance, i.e. to capture an additional construct of the gait function (Van Ancum et al., 2019). This information about gait performance is highly valuable for clinicians when devising a treatment plan such as adjusting a surgery. Furthermore, thanks to such assessments, clinicians could verify that the effect of a treatment ultimately generalizes into the child's daily life. Alternatives to the direct assessment of gait performance in daily life conditions, such as dual-task walking (Carcreff et al., 2019a; Katz-Leurer et al., 2014), or walking in semi-standardized or virtual reality environments (van der Krogt et al., 2014) can also be advised. Finally, therapists could also integrate day-to-day performance data into their training program plans in addition to body structures and functions.

Feedbacks on the feasibility of daily-life gait analysis

Although good acceptability of the measures was reported by participants and their families overall, daily-life assessments entail potential pitfalls. Indeed, a number of issues related to long-term measurements were reported in the diary or identified after data collection. The participants did not always follow the instructions to wear an Elastane sleeve or tight pants or socks to cover the sensors. The sensor fixation (PAL stickies, PAL Technologies Ltd., UK) alone was not sufficient. This problem was reported in 27% of the cases and was generally fixed by the participants with additional medical tape provided by the investigator. This should have been recommended from the beginning, as suggested previously (Del Din et al., 2016c). In the cases where the

sensor fell and was re-placed in a different orientation (i.e. visible by a change in the signs of the signals), the PCA calibration was repeated for the corresponding part of the data. Surprisingly, no issue was reported by the parents or the caregivers who were in charge of handling the sensors every evening and morning. Errors were found a posteriori, such as interruption of the measurement before reaching 10h of recording (7h50 in the worst case) most probably due to the child's timetable (13.1% of the recordings), and bad switch-off at the end of the day (3.6% of the recordings). Finally, 9.5% of the measurements were interrupted because of battery loss of at least one sensor (6h30 in the worst case). In any case, data was cut at the minimal time shared between the 4 sensors, resulting in an average of 11±2h of analyzed recordings per day. Globally, the feasibility of such assessments has been confirmed but several improvements need to be carried out, such as the sensor fixation, to enhance the usability of IMUs.

Study limitations

Additional study limitations need to be acknowledged. First, the sample size was low, only 29 participants, and may have weakened the statistical power of the analyses. However, the effect found in the CP group for the comparison between in-laboratory and daily life median speeds showed a medium substantial difference (effect size = 0.543) (Sullivan and Feinn, 2012) which is satisfactory for confidence in the results. Next, the description of the participant's ambulatory activities showed great differences between week-days and weekend days activities in both groups. This has previously been demonstrated for children with and without CP (Rowlands et al., 2008; van Wely et al., 2012). We chose to gather week-days and weekend days to have a global representation of daily life. Besides, limits related to the use of inertial sensors should be mentioned. Firstly, the calibration method based on PCA is not the most accurate approach from a biomechanical point of view. This method was adopted as an optimal solution since an approach based on functional calibration (Favre et al., 2009) using a pre-defined set of movements was difficult to be envisaged for children with functional disabilities, especially in the home environment without the supervision of the investigator. The PCA method is based on the assumption that the pitch angular velocity is maximal in the sagittal plane during forward walking. This assumption may have induced potential errors, with an impact on the computation of shank and thigh angles, hence on the walking speed estimation (Aminian et al., 2002), especially for the children with a high level of impairment, with higher frontal and transverse components at shank and thigh levels during walking. Second, precautionary measures were applied to avoid the inclusion of non-walking activity into the analysis. However, we cannot exclude erroneous inclusion of false positives, which can be responsible for the outliers in the speed distribution (Figure 50). Furthermore, the double pendulum model proposed by Aminian et al. (Aminian et al., 2002) relies on precise leg dimension (thigh and shank segment lengths) measurements that can be challenging with patients with bone deformities and joint contractures (Sabharwal and Kumar, 2008). This was also a potential source of errors. Only the right side was arbitrarily chosen, instead of the mean between the right and left sides, in order to avoid any erroneous calculation coming from right and left values belonging to non-successive steps. However, the results would have been similar with both methods since right and left strides parameters are theoretically identical. Last but not least, while walking speed in laboratory is estimated under same controlled conditions, walking speed in real-life condition is affected by the context changing the locomotion, e.g. due to crowd, weather, or path properties (Wang and Adamczyk, 2019). Moreover the power law distribution of walking bouts (Orendurff et al., 2008), involves much more short walking bouts in daily life corresponding mostly to indoor walking or walking in a room. This study lacks on context-related information to estimate the speed. This was partly compensated by the fact that only walking bout more that 10 steps were considered for comparison with laboratory trials. But 10 steps may represent more than the maximum number of steps taken in a row in the laboratory.

Perspectives for capacity vs performance comparison

The sensor configuration used in this study was more cumbersome than other single sensor configurations, such as trunk, waist or wrist-mounted sensors (Anisoara Paraschiv-Ionescu et al., 2019; Soltani et al., 2019; Zijlstra and Hof, 2003), but was chosen because it was demonstrated to be the most accurate system for walking speed estimation in children with CP (Carcreff et al., 2018). Furthermore, this configuration has the potential to quantify various other gait parameters that are of high interest to describe gait deviations like those of children with CP (Armand et al., 2016). The investigation of gait capacity versus performance based on multiple parameters constitutes a relevant perspective of this study in order to have a more detailed vision of the differences between clinical and daily life settings. Moreover, for a direct comparison between parameters assessed in the laboratory and in daily life, several approaches could be considered such as: including walking bouts with similar characteristics (distance, time or number of steps) to walking bouts in the laboratory, since bout length has an impact on gait characteristics (Del Din et al., 2016a); including frequently repeated walking bouts to eliminate unique behaviors or events from the analysis (Wang and Adamczyk, 2019); using technological developments such as multimodal sensing (e.g., GNSS, barometric pressure, microphone, weather records, etc.) to be more precise regarding the contexts, e.g. discriminate between indoor and outdoor, even and irregular surface, or straight and curved path, detect load carriage, a surrounding crowd or weather conditions (Wang and Adamczyk, 2019).

7.5 Conclusion

Walking speed was lower during natural walking as compared to laboratory-based walking in the group of children with CP. Speeds were also highly correlated which means that these children tended to under-use their gait capacity during daily life walking. In contrast, no difference was found between supervised and unsupervised walking in controls. Nevertheless, highly heterogeneous behaviors were observed at individual levels in both groups, and within GMFCS level sub-groups, which indicated that gait performance cannot be directly estimated from gait capacity. Overall, this study emphasizes the relevance of assessing natural walking as a complement to current capacity evaluations. Both assessments bring different and complementary information, which are valuable for clinicians, in the process of treatment planning and follow-up care.

Chapter 8 *

Laboratory versus daily life: multifeatures of gait

Abstract

Gait assessments in standardized settings, as part of the clinical follow-up of children with cerebral palsy (CP), may not represent gait in daily life. This study aimed at comparing gait characteristics in laboratory and real life settings on the basis of multiple parameters in children with CP and with typical development (TD). Fifteen children with CP and 14 with TD wore 5 inertial sensors (chest, thighs and shanks) during in-laboratory gait assessments and during 3 days of daily life. Sixteen parameters belonging to 8 distinct domains were computed from the angular velocities and/or accelerations. Each parameter measured in the laboratory was compared to the same parameter measured in daily life for walking bouts defined by a travelled distance similar to the laboratory, using Wilcoxon paired tests and Spearman's correlations. Most gait characteristics differed between both environments in both groups. Numerous high correlations were found between laboratory and daily life gait parameters for the CP group, whereas fewer correlations were found in the TD group. These results demonstrated that children with CP perform better in clinical settings. Such quantitative evidence may enhance clinicians' understanding of the gap between capacity and performance in children with CP and improve their decision-making.

* Chapter published as:
Carcreff L., Gerber C.N., Paraschiv-Ionescu A., De Coulon G., Newman C.J., Aminian K. and Armand S. « Comparison of gait characteristics between clinical and daily life settings in children with cerebral palsy », Scientific Reports, 2020, vol. 10, num. 2019. doi: 10.1038/s41598-020-59002-6 – with permission of all co-authors
My contributions: Methodology, recruitement, investigation, software, data curation, visualization, formal analysis, writing – original draft, writing-review & editing

8.1 Introduction

Cerebral palsy (CP) describes a group of motor disorders resulting from early damage to the developing brain (Baxter et al., 2007). It is the most frequent motor disability in children, with a prevalence of 1.8 per 1000 live births in Europe (Sellier et al., 2016). Children with CP have heterogeneous clinical profiles and are classified into five levels of severity with the Gross Motor Function Classification System (I: independent walker; II: independent walker with limitations; III: ambulate with walking aids; IV: ambulate with powered mobility; and V: dependent for all mobility) (Novak, 2014; Palisano et al., 1997). In CP, gait disorders are among the leading limitations, with a negative impact on participation and self-perception (Frisch and Msall, 2013). Current management of gait deviations is largely based on assessments of body structures and body functions of individuals measured in clinical settings (Gerber et al., 2019). 'Clinical gait analysis' (CGA) measures multiple gait parameters in order to identify and understand the main causes of gait deviations (Armand et al., 2016). Although CGA has become a widely accepted tool in clinical practice, it is not clear whether in-laboratory assessments reflect the usual walking performance of the patients in daily life. Patients are often considered to perform better when walking under clinical supervision to please caregivers (Toosizadeh et al., 2015), known as the 'Hawthorne effect' (Berthelot et al., 2011), and thanks to improved concentration in the absence of external distractors requiring additional attention (Gosselin et al., 2018). Integrating unsupervised assessments of the patients' daily walking into the clinical process could improve clinicians' understanding of their real behavior and overall difficulties, beyond the observation of functional limitations in a purely clinical setting (Gosselin et al., 2018).

The link between capacity (what an individual *can* do in a standardized environment) and performance (what an individual *does* do in his usual environment) (World Health Organization, 2002) remains a largely unsolved question (Holsbeeke et al., 2009). Various interpretations of capacity can be found in the literature. Capacity can be seen as the best possible level of functioning during short tasks (e.g. assessed by the Gross Motor Function Measure (GMFM) (Alotaibi et al., 2014) in CP), as the level of functioning during an endurance task (e.g assessed by the 1- or 6-Minute-Walk Test (1MWT or 6MWT) (Enright, 2003)) or as the spontaneous level of functioning during CGA (Wilson et al., 2014). For the latter, compound kinematic parameters, such as the Gait Deviation Index (GDI) or Gait Profile Score (GPS) (Schwartz and Rozumalski, 2008), were mostly reported (Guinet and Desailly, 2017; Nicholson et al., 2018; Wilson et al., 2015). Performance has mostly been assessed by self- or parent-report questionnaires about daily life mobility (Graham et al., 2004; Palisano et al., 1997), physical activity habits and activity limitations(Haley et al., 2010; Young et al., 2000). Thanks to the increasing availability of wearable motion sensors, objective data about performance is now accessible (Bjornson, 2019). Daily number of steps, time spent inactive and time spent in moderate-to-vigorous physical activities (MVPA) are common metrics used to quantify motor performance. Considering this high variety of metrics and definitions, no consensus has been found on the link between capacity and performance in children with CP. Capacity seems to exceed performance (Young et al., 1996), however this relationship is not constant over time and across all GMFCS levels (Ho et al., 2017; Van Gorp et al., 2018). Low to moderate correlations between capacity and performance were found in the majority of studies (Guinet and Desailly, 2017; Mitchell et al., 2015b; Nicholson et al., 2018; Wilson et al., 2015; Wittry et al., 2018).

Gait characteristics are measured in the context of a walking activity which can be performed in a standardized environment, e.g. during CGA, then called walking capacity, or in a usual environment, then called walking performance. Gait characteristics are related to the body functions (gait pattern functions as classified in the ICF, WHO (Bertuletti et al., 2019)), in opposition to gait quantity which is rather associated with the amount and intensity of the ambulatory activity. The previously-mentioned studies essentially demonstrated that gait characteristics (GDI, GPS, walking speed) measured in the laboratory cannot predict gait quantity in daily life

(Brandes et al., 2008). To date, data on gait characteristics in daily life settings is lacking, and could bring additional valuable insights into the motor performance of children with CP.

Gait can be described by multiple features since it involves various physiological systems (Bonnefoy-Mazure et al., 2015). Distinct domains can depict gait function such as pace, rhythm, variability, asymmetry, postural control, amplitude, etc. (Ben Mansour et al., 2017; Lord et al., 2013; Thingstad et al., 2015). In the context of CGA, spatiotemporal, kinematic, kinetic parameters, among others, are commonly assessed. Motion sensors such as Inertial measurement units (IMU) can quantify several of these gait parameters with a good level of accuracy in pathological populations (Jarchi et al., 2018; Petraglia et al., 2019; Vienne et al., 2017). In children with CP, few sensor configurations have been tested. Foot placement accurately estimates spatiotemporal parameters in children with a low level of disability (Brégou Bourgeois et al., 2014), while sensors on the lower limbs (shanks and thighs) demonstrated better accuracy for speed estimation in children with higher levels of disability (GMFCS III) (Carcreff et al., 2018). A sensor located on the trunk was also found to appropriately measure parameters of postural control (Chen et al., 2017; Saether et al., 2014) and to accurately estimate cadence (Anisoara Paraschiv-Ionescu et al., 2019). IMUs have the potential to assess gait characteristics in real life settings and to enable direct comparisons with gait measured in the laboratory.

The purpose of this study was to compare gait characteristics between laboratory and real life settings on the basis of multiple features representing different aspects of gait, in children with CP and typical development (TD). The comparisons were based on the evaluation of the difference and the association between parameters in both environments at the group level.

8.2 Method

8.2.1 Participants

This observational cross-sectional study included a convenience sample of patients diagnosed with CP and followed at the Geneva University Hospitals, aged between 8 and 20 years and with a level of gross motor function (GMFCS) between I and III, meaning that they were able to walk independently with or without mechanical assistance. A group of TD children were also recruited, similar in age and sex. The exclusion criteria for both groups were the standard criteria that preclude adequate participation to the requested tasks, such as significant behavioral issues, severe visual disorders, attention deficit or mental age inferior to 8 years. The protocol was approved by and carried out in accordance with the hospital's institutional ethical committee (Cantonal Commission for Research Ethics of Geneva - CCER-15-176). Informed consent was obtained from a parent, a legal guardian or the participant him/herself (if older than 18 years).

8.2.2 Measurement protocol

This study protocol was twofold. First, the participants performed barefoot standard gait assessments in the laboratory with the instruction to "walk as usual, as if you were in the street", as in a CGA protocol. Several (between 4 and 10) back and forth walking trials over a 10-meter walkway were performed. Second, the participants were monitored during 3 days including 2 school days and one day of the weekend, for at least 10 consecutive hours. During both assessments, five synchronized IMU-based devices (Physilog4®, GaitUp, Switzerland) were fixed on the lower limbs (shanks and thighs) and on their chest (Figure 51). Each IMU comprised a triaxial accelerometer (range ±16g), and triaxial gyroscope (range ± 1000°/s) with a sampling frequency of 100 Hz. For the in-laboratory measurements, the IMUs were fixed by the investigatorwith hypoallergenic adhesive films (Opsite Flexigrid, Smith & Nephew Medical, UK). At the beginning of each day of daily life measures, the IMUs were placed by the parents or caregivers, who received practical training

(as well as a user guide to support them at home) from the investigator for the IMUs management and placement, with hypoallergenic double-sided hydrogel stickies (PAL stickies, PAL Technologies Ltd., UK). The IMUs were also protected from falling with a handmade Elastane sleeve, or under tight pants and socks. At the beginning of the first (laboratory) assessment, a trained investigator measured anthropometric values (shank and thigh lengths) and lower limb muscle strength (using the Medical Research Council testing (Florence et al., 1992)) for each participant. The delay between the two assessments was of 7±3 months, since the laboratory measurements were performed within an initial technical validation study (Carcreff et al., 2018) and daily life measurements in subsequent reliability (Gerber et al., 2019) and interventional studies, constrained by school holidays and logistic issues (number of available sensors). None of the children underwent surgery or intensive therapy between both measurements.

8.2.3 Pre-processing

Laboratory measures: IMU data recorded continuously by all devices was automatically cropped into several walking episodes (corresponding to each back and forth trial on the walkway in the laboratory, i.e. excluding turns). To guaranty reproducible measure and be independent of the IMU location on each segment, lower limbs sensors were automatically aligned with the functional axis of the movement. To this end, assuming that the main angular rotation during gait occurs around the medio-lateral axis of each segment, principal component analysis (PCA) was applied on angular velocity to assess the pitch component of the shanks and thighs rotation (Falbriard et al., 2018; Mcgrath et al., 2018). For each trial, the norm of acceleration of the chest was computed, to preclude wrong axis selection resulting from potential misalignment of the sensor with regard to the chest.

Daily-life measures: Walking episodes were detected within the continuous daily recording using the pitch angular velocity of both shanks based on the method described by Salarian et al. (2004). The 3D signal of the longest detected walking bout (WB) was used to determine the PCA coefficients; then, axis alignment was performed on the entire signal to extract the pitch angular velocity, as for the laboratory assesment. The norm of acceleration of the chest was also computed for each WB. Only WBs with a minimum of 8 steps were considered for the next steps, to preclude from the inclusion of too short WB.

8.2.4 Walking bout selection

Since in the laboratory the instruction was to walk continuously along a 10-meter walkway, in this study we included daily life WBs with a travelled distance corresponding to approximately 10 m (from 5 to 15 m), without breaks or aberrant gait cycles (resulting from false positive detected gait cycles), in order to represent similar conditions.

Thresholds for break and aberrant gait cycle definitions were set based on data collected during the standard laboratory assessment at various speeds, with the same study participants. Details are provided in the **Appendix**.

Included WBs were then further characterized as described in the next section, and compared with the WBs in the laboratory. An overview of data processing is presented in Figure 51.

8.2.5 Walking bout characterization

This study sought to characterize gait function through several aspects, called ‘domains’. For each domain, a very large number of variables could have been considered so we chose the ones that were the most used in the literature, and we applied some ‘rules’. The common rules for parameters inclusion were: to avoid duplication of parameters from one domain to another, and to avoid redundancy of parameters within the same

domain (Lord et al., 2013). Therefore, based on the literature (Ben Mansour et al., 2017; Del Din et al., 2016a; Lord et al., 2013) and the potential of IMU data, eight gait domains with the corresponding parameters were defined, as follows. For bilateral parameters, only the more affected side (based on muscular strength of the lower limbs) of children with CP, and arbitrarily, the left side for TD children, was selected for WB characterization.

Rhythm: Following the detection of right and left 'foot strike' and 'foot off' events on the shank pitch angular velocity signals (using the method described by Salarian et al. (2004)), the following temporal parameters of gait were computed: stride time and stance time (as a percentage of stride time). Swing time and cadence were redundant information (since swing time = (stride time – stance time) and cadence = (120/stride time)), so they were not reported.

Pace: Stride length was computed from the pitch angular velocity of the shanks and thighs, based on the double pendulum model introduced by Aminian et al. (Aminian et al., 2002; Salarian et al., 2004). This model uses thigh and shank lengths and orientations (computed by the numerical integration of pitch angular velocities) at foot strike and foot-off instants of time. Walking speed was computed as the ratio between stride time and stride length.

Amplitude: The knee flexion-extension angle was computed by the difference between shank and thigh angles (Salarian et al., 2004). This parameter has been described as highly representative of the gait pattern of children with CP (Bonnefoy-mazure et al., 2013; Rodda et al., 2004; Sutherland and Davids, 1993). The ranges of motion (ROM) over the gait cycle were computed.

Stability: The time of double support (when both feet are on the ground) as a percentage of the stride time was computed. This outcome was found to be increased in the children with CP in order to ensure better stability (Brégou Bourgeois et al., 2014). Furthermore, for stability assessment, the standard deviation of the norm of chest acceleration was computed (Trunk $Acc._{SD}$) (Menz et al., 2003). Standard deviation (dispersion relative to zero) was chosen instead of root mean square (dispersion relative to the mean) to remove the gravity component (Menz et al., 2003).

Coordination: The walk ratio was described as a simple index for temporal and spatial coordination description, independent from walking speed (Sekiya et al., 1996; Sekiya and Nagasaki, 1998) and as an outcome measure for treatments aiming at improving motor coordination (Rota et al., 2011). Since step length was not computable with our system, the walk ratio as described by Sekiya et al. (Sekiya and Nagasaki, 1998) was computed using the ratio between stride length and cadence. Furthermore, the cyclogram has previously been described as a marker of coordination in subjects with total hip arthroplasty (Longworth et al., 2018), knee-amputees and adults with CP (Hershler and Milner, 1980). The area and the perimeter of the shank-thigh elevation angle cyclogram were computed. The ratio between the cyclogram perimeter and the root mean square of the cyclogram area was used as a coordination parameter (Goswami, 1998).

Smoothness: The smoothness of a movement can be affected by spasticity which is a major issue in CP (van den Noort et al., 2009). Higuchi's fractal (Higuchi, 1988) dimension was used for this purpose in children with hemiplegia to assess the smoothness/roughness of the affected upper limb (Newman et al., 2017). Fractal dimension was computed on the shank pitch angular velocity time series, for each gait cycle.

Variability: Gait variability is known to be higher in children with CP than TD peers in a clinical context (Brégou Bourgeois et al., 2014; Steinwender et al., 2000). Inter-cycle variability was computed as the standard deviation for the rhythm and pace parameters (Morris et al., 2017). The standard deviation was preferred to the coefficient of variation (=standard deviation/mean x 100) for better interpretability and to avoid extreme values due to low means (Lord et al., 2011).

Asymmetry: Symmetry is a good indicator of gait efficiency (Ben Mansour et al., 2017) and is particularly impaired in the population with unilateral CP (Saether et al., 2014). The symmetry index (Blazkiewicz et al., 2014) was computed for the stance time and knee angle since they represent step parameters (in opposition with stride parameters which combine right and left sides). The symmetry index was chosen since it was demonstrated to be the most sensitive to detect gait asymmetry from spatiotemporal parameters in healthy subjects, and the most commonly used in studies reporting symmetry (Blazkiewicz et al., 2014). The limp, representing the difference between the initial and terminal double support, was also computed (Salarian et al., 2004)

8.2.6 Data analysis

Non-parametric tests were used in light of the small sample size. Paired Wilcoxon tests were used to compare the medians of laboratory and daily-life gait parameters. Spearman's correlation coefficients (rho) were computed between the laboratory and the daily-life gait parameters. Altman's guidelines were used to interpret the correlation: poor, if $rho<0.20$; fair, if $0.20\leq rho<0.40$; moderate, if $0.40\leq rho<0.60$; good, if $0.60\leq rho<0.80$; and very good, if $rho\geq0.80$ (Altman and Altman, 1999). Alpha was set at 0.05, and the results with Bonferroni's correction were also presented. Effect size was computed by dividing the Wilcoxon test statistic by the square root of the number of observations, as suggested by Pallant et al. (2013).

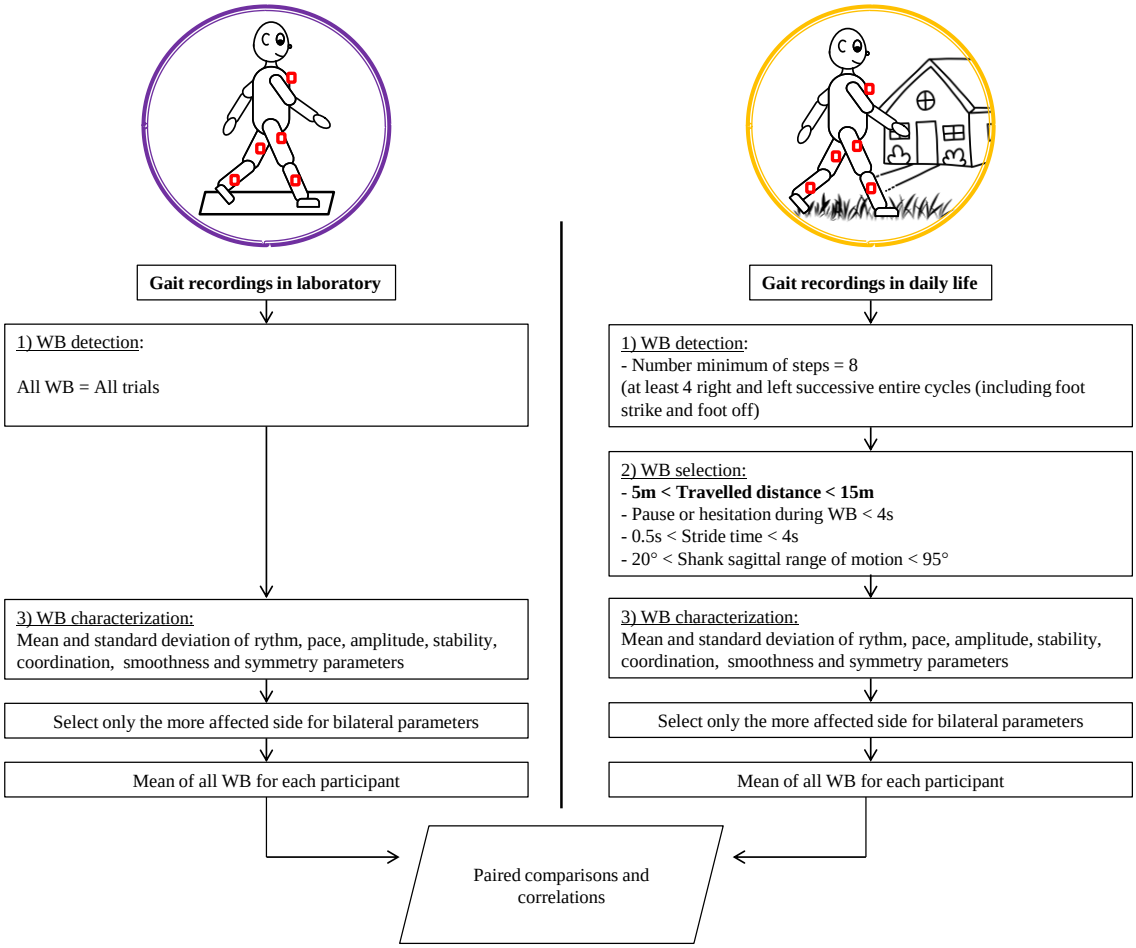


Figure 51 – Sensor configuration and flowchart for data processing regarding walking bout (WB) detection, selection and characterization

8.3 Results

8.3.1 Participants' characteristics and ambulatory activity

Fifteen children with CP and 14 children with TD were included. One child with CP – GMFCS III had only one WB exceeding 5m so we chose to exclude her for further analysis. Therefore, the remaining participants' characteristics are presented in Table 21. The dominant clinical presentation of participants with CP was spastic diplegia (n=12) and 50% of them needed a walking aid (crutches or walker) to ambulate in the community.

The number of detected WB, the median and maximal distance per WB are shown in Table 21. We observed that children with CP – GMFCS II and III walked less than 5m in most of their daily WB. The number of WB included following our criteria of selection (i.e. 5 to 15m) corresponded approximately to 30% of the detected WB for each group.

Table 21– Participants characteristics and proportion of included daily life WB

	CP (n=14)				**TD (n=14)**
Age (years)	12.6 [11.4-13.9]				12.3 [11.5-14.5]
Height (m)	1.51 [1.38-1.60]				1.57 [1.47-1.66]
Weight (kg)	43.5 [36.0-50.5]				45.7 [37.7-57.0]
Sex (number of girls)	8				8
	ALL (n=14)	GMFCS I (n=6)	GMFCS II (n=3)	GMFCS III (n=5)	
Number of detected WB	211 [113-238]	237 [224-271]	183 [139-279.5]	113 [90-113]	335 [265.5-499]
Median distance travelled / WB (m)	6.4 [4.9-7.3]	13 [12-14]	4.9 [4-7]	5.0 [4.1-5.4]	12 [12-14]
Maximal distance / WB (m)	209.4 [48.8-433.1]	420.9 [363.4-464]	322.4 [185.5-505.7]	47.6 [37.7-50.0]	558.7 [375.6-658.3]
Number of included WB (% of detected WB)	30.3 [28.6-35.6]	31.7 [29.7-36.4]	28.5 [20.6-30.6]	30.0 [28.9-36.3]	31.5 [27.4-34.3]

Results are presented as medians [IQR] of the group

8.3.2 Laboratory versus daily life

The results of the comparisons between gait parameters in laboratory and in daily life are presented in Table 22 and illustrated in Figure 52Figure 51 with radar plots for each group. Scatterplots for each parameter, with the distinction of the 2 groups (CP and TD) and the GMFCS levels can be found in Figure 53. There was a high inter-subject heterogeneity within the CP group for both settings as represented on Figure 52.

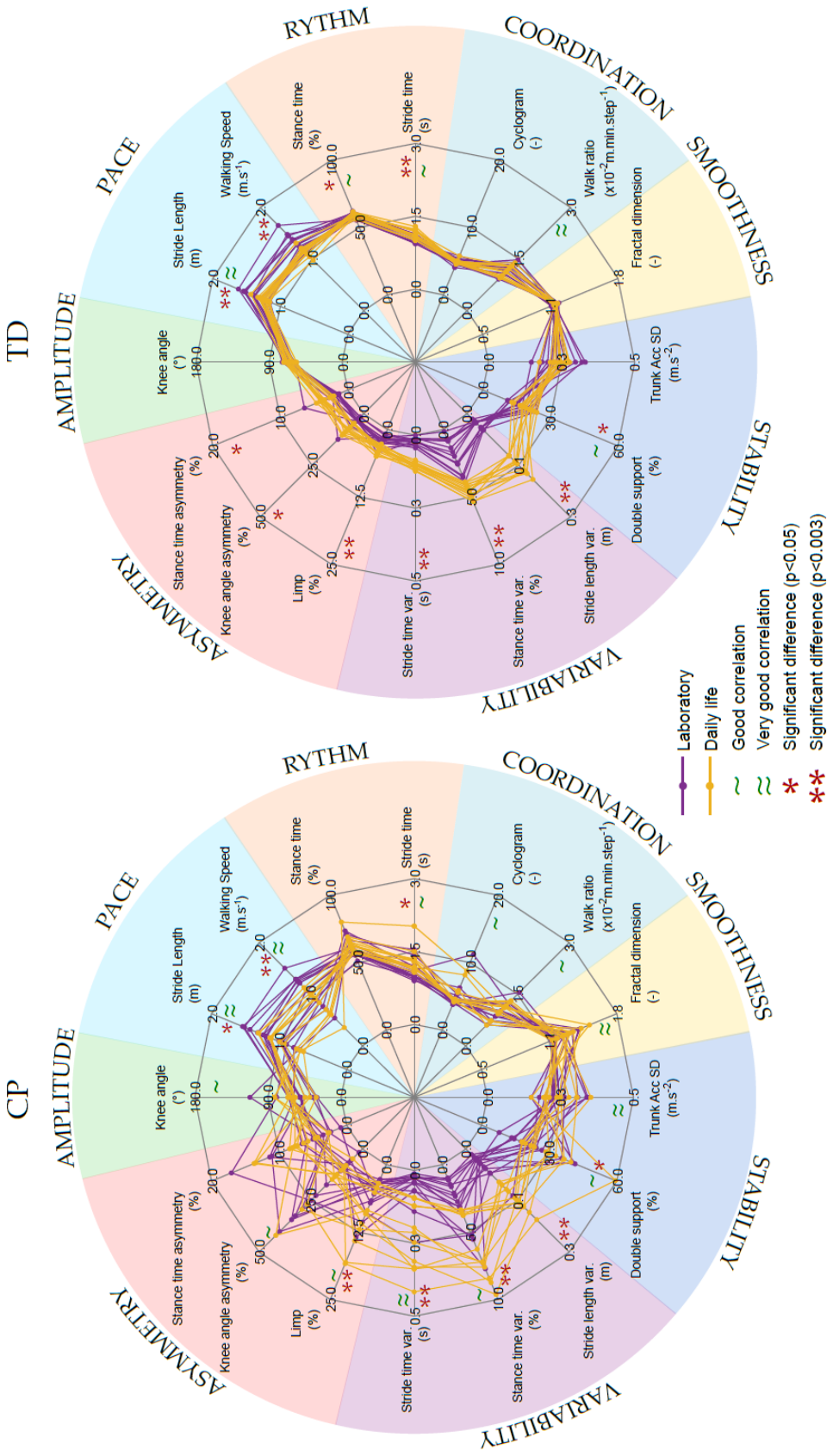
In both groups, all the parameters belonging to the pace and variability domains were significantly ($p<0.011$) different between the laboratory and daily life measures; the variability being higher in daily life while the speed was lower. The difference was more pronounced for TD where also rhythm and asymmetry domains were significantly ($p<0.035$) different between the two settings. In both groups, no difference was found for the amplitude, smoothness and coordination domains, while only double support was found increased in the stability domain.

In CP, most of the assessed gait parameters across all domains in daily life had good to very good correlations with the parameters in the laboratory (12/16 parameters with rho≥0.60). The highest correlations (rho≥0.80) were found for speed, stride length, stride time variability, trunk $acc._{SD}$ and fractal dimension. In TD however, correlations were less manifest and fewer parameters were correlated (5/16 parameters with rho≥0.60) between the laboratory and the daily life. No significant correlation was found in the amplitude, asymmetry, variability, and smoothness domains.

Table 22– Laboratory and daily-life based gait parameters for each group

		Laboratory		Daily life		Paired comparison			Correlation	
	Variable	**median**	**IQR [Q1:Q3]**	**median**	**IQR [Q1:Q3]**	**p.value**	**es**	**95% CI**	**rho**	**p.value**
CP (n=14)	**RYTHM**									
	Stride time (s)	1.03	[0.98:1.18]	1.25	[1.18:1.32]	**0.004**	0.501	[-0.25:-0.09]	0.72	**0.005**
	Stance time (%)	58.95	[56.83:62.77]	62.52	[58.13:65.21]	0.119	0.223	[-5.51:0.48]	0.53	0.057
	PACE									
	Speed ($m.s^{-1}$)	1.15	[0.84:1.27]	0.91	[0.65:1.01]	**0.002***	0.553	[0.09:0.26]	0.85	**<0.001***
	Stride length (m)	1.09	[0.93:1.30]	1.12	[0.79:1.14]	**0.011**	0.435	[0.03:0.18]	0.88	**<0.001***
	AMPLITUDE									
	Knee angle (°)	53.97	[45.78:64.25]	60.19	[52.28:63.6]	0.296	0.101	[-7.76:3.12]	0.75	**0.003***
	ASYMMETRY									
	Stance time asy. (%)	4.34	[2.66:5.62]	6.05	[4.41:7.88]	0.194	0.163	[-4.5:0.53]	-0.05	0.868
	Knee angle asy. (%)	9.89	[7.61:27.5]	12.47	[9.16:14.39]	0.903	0.246	[-4.37:8.2]	0.56	**0.042**
	Limp (%)	4.43	[3.43:6.97]	8.76	[4.26:11.75]	**0.002***	0.535	[-4.74:-1.15]	0.65	**0.014**
	VARIABILITY									
	Stride time var. (s)	0.03	[0.02:0.06]	0.21	[0.12:0.33]	**<0.001***	0.693	[-0.22:-0.1]	0.90	**<0.001***
	Stance time var. (%)	2.90	[1.51:3.78]	6.17	[3.74:7.26]	**<0.001***	0.659	[-4.09:-2.16]	0.74	**0.004**
	Stride length var. (m)	0.04	[0.03:0.05]	0.14	[0.12:0.16]	**<0.001***	0.693	[-0.12:-0.08]	0.03	0.928
	STABILITY									
	Double support (%)	22.49	[15.62:26.1]	25.94	[20.05:35.59]	**0.035**	0.342	[-9.5:-0.24]	0.64	**0.017**
	Trunk $Acc._{SD}$ ($m.s^{-2}$)	0.24	[0.20:0.26]	0.2317	[0.20:0.27]	0.626	0.061	[-0.02:0.01]	0.91	**<0.001***
	SMOOTHNESS									
	Fractal dimension (-)	1.28	[1.21:1.33]	1.28	[1.20:1.30]	0.903	0.246	[-0.02:0.02]	0.93	**<0.01**
	COORDINATION									
	Walk ratio ($x10^{-2}$ $m.min.step^{-1}$)	1.01	[0.88:1.19]	1.1	[0.94:1.17]	0.855	0.2	[-0.09:0.11]	0.74	**0.004**
	Cyclogram (-)	4.58	[4.11:5.30]	4.49	[4.36:5.10]	0.808	0.164	[-0.54:0.53]	0.74	**0.004**
TD (n=14)	**RYTHM**									
	Stride time (s)	1.07	[0.98:1.11]	1.12	[1.08:1.21]	**0.001***	0.573	[-0.12:-0.05]	0.75	**0.003***
	Stance time (%)	58.14	[57.05:60.46]	59.43	[58.64:60.78]	**0.035**	0.342	[-1.87:-0.23]	0.78	**0.002***
	PACE									
	Speed ($m.s^{-1}$)	1.28	[1.18:1.38]	1.15	[1.11:1.19]	**0.001***	0.573	[0.08:0.24]	0.29	0.318
	Stride length (m)	1.38	[1.25:1.49]	1.26	[1.20:1.30]	**0.001***	0.573	[0.06:0.16]	0.87	**<0.001***
	AMPLITUDE									
	Knee angle (°)	66.18	[62.63:66.81]	66.97	[63.44:68.71]	0.542	0.02	[-4.34:2.78]	0.28	0.325
	ASYMMETRY									
	Stance time asy. (%)	1.69	[1.46:2.25]	3.65	[2.90:3.92]	**0.011**	0.435	[-1.94:-0.84]	0.42	0.141
	Knee angle asy. (%)	3.33	[2.89:3.56]	7.40	[5.00:8.05]	**0.005**	0.484	[-4.71:-1.54]	0.15	0.605
	Limp (%)	2.03	[1.62:2.57]	3.49	[3.20:4.017]	**0.002***	0.535	[-2.07:-0.95]	0.29	0.318
	VARIABILITY									
	Stride time var. (s)	0.02	[0.02:0.03]	0.10	[0.10:0.11]	**<0.001***	0.693	[-0.09:-0.08]	0.07	0.820
	Stance time var. (%)	1.83	[0.83:2.56]	4.52	[4.16:4.83]	**<0.001***	0.693	[-3.28:-1.96]	0.20	0.483
	Stride length var. (m)	0.03	[0.03:0.04]	0.15	[0.13:0.17]	**<0.001***	0.693	[-0.13:-0.10]	0.35	0.215
	STABILITY									
	Double support (%)	16.48	[14.56:20.05]	18.79	[17.04:21.02]	**0.020**	0.387	[-3.45:-0.38]	0.78	**0.001***
	Trunk $Acc._{SD}$ ($m.s^{-2}$)	0.23	[0.21:0.26]	0.25	[0.22:0.26]	0.808	0.164	[-0.04:0.03]	0.35	0.221
	SMOOTHNESS									
	Fractal dimension (-)	1.20	[1.18:1.21]	1.20	[1.19:1.21]	0.54	0.02	[-0.02:0.01]	0.49	0.075
	COORDINATION									
	Walk ratio ($x10^{-2}$ $m.min.step^{-1}$)	1.22	[1.10:1.31]	1.13	[1.00:1.29]	0.07	0.282	[0.00:0.11]	0.81	**0.001***
	Cyclogram (-)	4.64	[4.54:5.14]	4.88	[4.73:5.00]	0.39	0.052	[-0.29:0.13]	0.58	**0.033**

*Var: variability; Asy: Asymmetry; Acc: acceleration; SD: standard deviation; es: effect size, P-values in bold are <0.05, and a * is indicated if the level of significance after Bonferroni correction (0.003) is reached.*



*Each curve represents a participant. Significant differences at the group level between in-laboratory and daily-life gait parameters are marked with * if p<0.05 and with ** if p<0.003 on the corresponding axis. Significant and good correlation (p<0.05, rho>0.61) are marked with ~ and very good correlations (p<0.003, rho>0.81) are marked with ≈ on the corresponding axis*

Figure 52 - Radar plots presenting the 16 gait parameters (8 gait domains) assessed in laboratory (purple curves) and in daily-life (yellow curves) for the CP and the TD groups

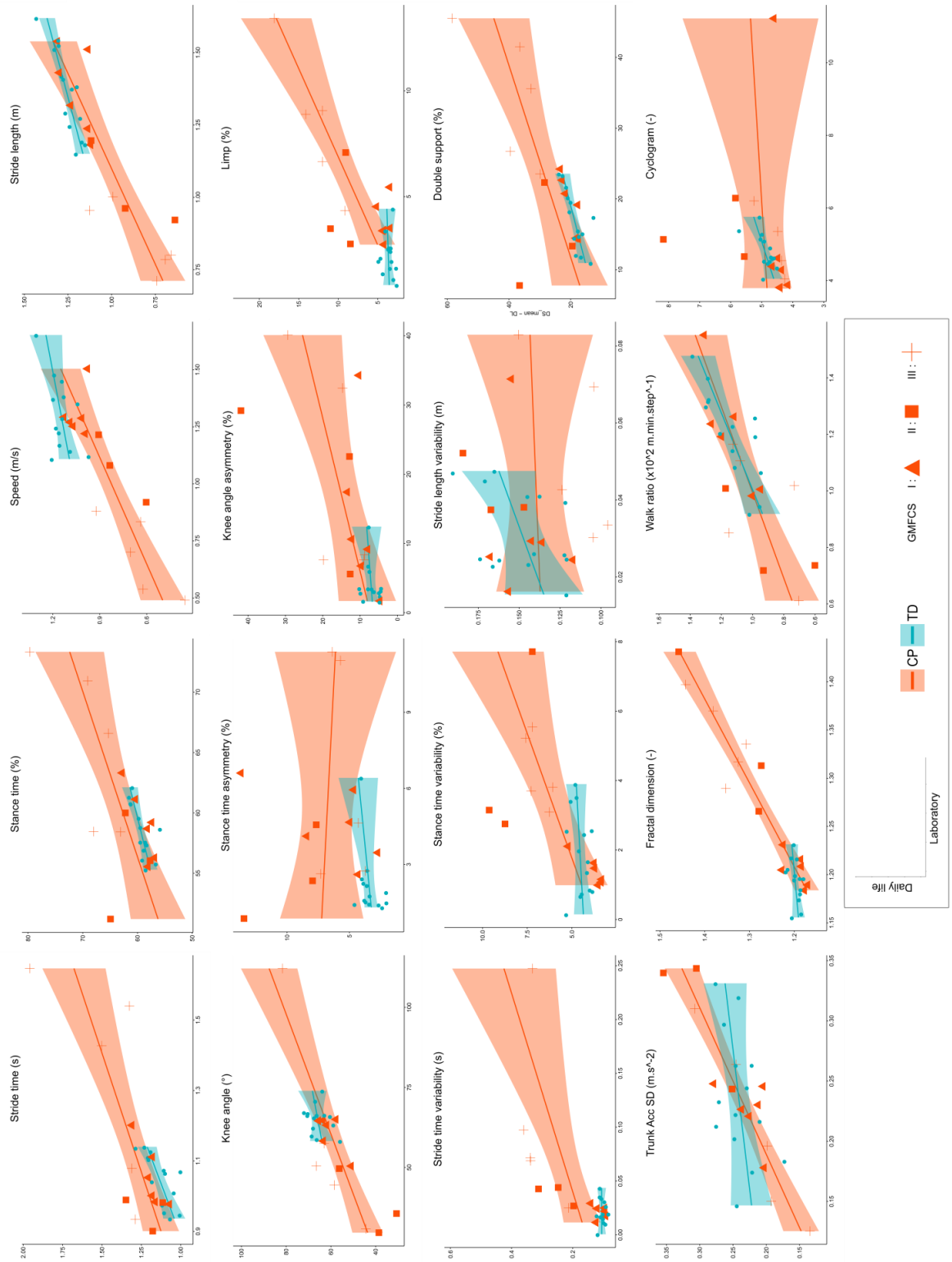


Figure 53 - Scatterplots representing the relationships between gait parameters measured in daily life and in laboratory for children with cerebral palsy (CP) and typical development (TD)

8.4 Discussion

The objective of this study was to compare multiple gait parameters between two distinct environments: the laboratory where the participant is sought to demonstrate the best of himself (Berthelot et al., 2011) (which can be seen as 'walking capacity'), and real life where the actual walking habits ('walking performance') can be observed. The main findings were that 1) in contrast to TD, most of the gait parameters of children with CP were correlated between both environments, and 2) for both groups substantial differences were found between the settings for most of the parameters, capacity exceeding performance.

While previous studies also emphasized differences between capacity and performance when comparing laboratory and daily life assessments, our findings suggest a certain correlation between gait parameters obtained in laboratory and daily life conditions, which is in contrast to previous findings (Guinet and Desailly, 2017; Mitchell et al., 2015b; Nicholson et al., 2018; Wilson et al., 2015; Wittry et al., 2018). The discrepancy can be explained by the dissimilar definitions and metrics used to reflect walking capacity and performance. When gait characteristics evaluated in the laboratory at highest or spontaneous level of functioning was compared to gait quantity in daily life (e.g. total number of daily steps, % spent in MVPA), no correlation was found, involving that CGA cannot be used to estimate daily life quantity of activity (Brandes et al., 2008). The strength of our study was to compare (i) the exact same metrics of gait and (ii) during similar length of WB in both environments, and high correlations for the majority of parameters in CP were found. This indicates that a child with CP showing higher values in gait parameters measured in the laboratory most probably shows higher values in the same gait parameters in daily life.
As compared to the CP group, children with TD had fewer correlations between gait parameters in the laboratory and daily life. First, this can be due to the values' heterogeneity in the CP group, favoring correlations, as illustrated in supplementary Fig. S1 (for example, walking speed ranged between 0.65 and 1.27 m/s in CP, whereas it ranged between 1.10 and 1.38 m/s in TD). Second, this can be the reflection of better capability of children with TD to adapt their gait to the context. This is in agreement with Gosselin et al. who stated that individuals with decreased capacity may have difficulties to efficiently respond to unpredictability (Gosselin et al., 2018).

In general, gait function of children with CP and children with TD changed in the same direction, i.e. for instance, higher variability, lower speed, higher asymmetry, and lower stability in daily life. However, there where less gait parameters with significant differences between the laboratory and daily life in children with CP compared to the TD group. This was mostly due to the heterogeneity among children with CP. In fact, greater variations of the parameters were found in the CP group, than in the TD group. As an example, the stance duration increased by 3.6% but was not significant ($p=0.119$) at the CP group level, as compared to 1.3% which was significant ($p=0.035$) at the TD group level.

This study was the first to compare laboratory versus daily life gait characteristics using identical metrics belonging to various domains in children. Although mostly correlated, not all the gait characteristics in children with CP revealed to be different between both contexts of walking. The results showed that the amplitude, smoothness and coordination domains were similar between both environments for both groups. High correlations were also found in these domains in children with CP, implying that these domains are inherent to their gait pattern independently of the walking context. Van der Krogt et al. had similar findings when simulating an external environment with virtual reality (VR) (van der Krogt et al., 2014), and comparing kinematic parameters (amplitude domain) of gait during VR and CGA protocols. The variability and asymmetry of gait were higher in daily life in both groups. This was expected since the environment and tasks

are more variable in daily life (curved trajectories, inclined or uneven surfaces, obstacles, dual tasking, etc). However, asymmetry of gait in children with CP did not increase as much as for TD children, so they might have stayed on safer and more regular paths. The stability tended to decrease in daily life in both groups but not as significantly as the variability. This was in line with the study of Tamburini et al. which showed that the regularity of gait was highly altered by the testing conditions and environments, whereas the stability was not (Tamburini et al., 2018). Finally, pace and rhythm were influenced by the real life context, especially in the TD group with highly significant increases of stride time and stance duration and decreases of speed and stride length. The decrease of speed was due to both decreased stride length and increased stride time (i.e. decreased cadence) in TD, while in CP increase of stride time (i.e. decreased cadence) was the main cause of slower speed. Results in the rhythm domain were also verified in a recent study of Bisi et al. assessing children with TD between 6 and 25 years-old in natural and tandem, reflecting challenging walking (Bisi et al., 2019).

This was the first study to select daily life WB according to the distance travelled. Indeed, the original purpose was to use comparable conditions, using similar metrics. Several previous studies attempted to compare gait parameters in clinical with free-living settings but did not take the WB properties into account. However, regardless of pathology, WB length has a high impact on gait parameters (Del Din et al., 2016a; Orendurff et al., 2008). In a study with patients with Parkinson's Disease, Del Din et al. described that gait characteristics in free-living conditions approximated the values of laboratory setting when the duration of the WB corresponded to the time of the laboratory testing protocol (Del Din et al., 2016a), whereas, for other WB lengths, substantial differences and low to moderate correlations for all gait parameters (14 parameters) were found. Selection of WBs may thus be of high importance when comparing laboratory and daily life gait characteristics. Removing curved gait from the WB selection should also be considered in future studies. In this study, only the pitch axis of the gyroscope was aligned with the mediolateral anatomical axis, since functional calibration tasks were difficult to ask to the children, parents or caregivers during the daily-life measurements. The signals in the two other dimensions, which could have been used to determine turning gait, were not used.
Considering the distance criteria for WB inclusions, about 30% of daily life WBs was found to represent the laboratory conditions (standard for all laboratories performing CGA (Baker, 2013)) in each group. Our results also indicated that these 30% of WBs might represent the longest (in distance) WBs for children with CP, especially those with a higher level of disability (GMFCS II and III), whereas they could represent the median WB distance for children with TD and for children with CP with a low level of disability (GMFCS I). This is in agreement with previous studies stating that children with TD are more active on a daily basis (Bjornson et al., 2007).

The findings of this study should be interpreted in light of its limitations. First, a low number of participants were included, lowering the statistical power of the analyses. To help the readers to interpret the significance of the results, effect sizes were reported and the interpretation of p-values can be adjusted according to Bonferroni corrections. Increasing the sample size could have strengthened the conclusions and allowed to divide the CP group into subgroups of severity of the disability (GMFCS levels or laterality of the impairments). In addition, non-parametric tests were performed due to the low sample size. Confounding parameters such as age, sex, height, and weight, which were not adjusted for the model, may have influenced the correlations. Further work investigating this aspect on a bigger cohort should be undertaken.
Laboratory and daily-life assessments were performed months apart. Even if gait is supposed to be stable at this age, this could have introduced bias due to limited changes in morphology which could induce minor changes in the gait pattern.

Next, in this study, only WBs with similar length than laboratory walking were analyzed. This was the chosen solution to make reasonable comparisons of gait characteristics between two contexts of walking. However, clinicians might not only be interested in « short » WBs, especially for children with GMFCS I. Hence, this kind of assessment is intended to be complementary to gait quantity evaluation. Knowing the qualitative parameters that limit gait quantity on a daily basis could indeed be of high interest, especially for the therapists. This could inform them about which gait characteristics should be improved to potentially augment walking quantity.

Regarding IMUs use, the sensor frame alignment was only based on PCA and no conventional functional calibration was performed since the parents or the caregivers mounted the system during the home-based measurements. The PCA axis alignment may have introduced a small bias especially for the children with GMFCS III where transverse and frontal components in the gait pattern are higher than for non-pathological gait. This may have influenced the results of gait parameters in the amplitude, pace, coordination and asymmetry domains for which the angular velocity rate was used for their computation. In addition, the double pendulum model proposed by Aminian et al. (Aminian et al., 2002) relies on precision of leg dimensions (thigh and shank segments lengths) measurements. Although such a measurement with a tape has proven acceptable validity and reliability, potential sources of error can arise when doing the measures on patients with bone deformities and joint contractures (Sabharwal and Kumar, 2008).

Finally, through this study, the feasibility of using IMUs to measure objective parameters of gait function in daily life settings have been confirmed. Children showed an overall good acceptability of wearing the sensors since they did not report major issues. However, among all days of measurements, in 27% of the cases, at least one sensor fixation (PAL stickies, PAL Technologies Ltd., UK) was reported deficient. The problem was fixed by the participants with additional medical tape provided by the investigator. The parents and the caregivers did not report any troubles handling the sensors. Among the total days of measurement, 13.1% were interrupted before reaching 10h of recording (7h50 in the worst case) by the parent or the caregiver, 9.5% of the measurements were interrupted because of battery loss of at least one sensor (6h30 in the worst case), and 3.6% of the measurements had at least one sensor wrongly switched off at the end of the day. In all of these cases, we cut the data at the minimal time between the 5 sensors, resulting in an average of 11±2h of analyzed recordings per day. Several improvements need to be carried out to maximize the potential of IMUs, e.g. by minimizing the number of sensors and improving the sensor fixation to increase acceptability and performing a complete sensor calibration to compute absolute angles.

This study highlighted the relevance of wearable gait analysis to improve clinical decision making by considering free-living parameters. Clinical decision making is indeed mainly based on 3D motion analysis performed in laboratory settings, when real-life outcomes are the most determinant for children and their families. Tracking gait function in daily-life thanks to IMUs ensures that the effects of clinical decisions ultimately generalize into daily settings. Moreover, IMUs are nowadays close to provide data equivalent to optoelectronic systems, especially kinematics (Cutti et al., 2010), but need more validations in pathological populations like CP. IMUs have thus the potential to provide a fast, cost-efficient and especially accessible CGA, which are for now restricted to small selection of clinicians due to high costs in material and resources. To conclude, IMUs are now ready to complement 3D gait analysis, and may eventually replace optoelectronic systems once more validation studies will demonstrate their ability to compute kinematics and kinetics. This will open the possibility to perform CGA not only in gait laboratories but also in local medical care settings.

8.5 Conclusion

Gait characteristics assessed in a clinical context appeared highly associated with gait characteristics in a daily life context in children with CP, which was less evident for children with TD. Most gait characteristics differered between both environments (laboratory vs daily life) in both groups. Parameters assessed in the laboratory exceeded the parameters measured in daily life (increased stride time, decreased speed, increased asymmetry, etc.). The present results proved with objective and quantitative evidence that children with CP perform better in clinical settings. Overall, these exploratory findings emphasized the importance of performance considerations in future clinical research to improve clinicians' understanding of the gap between capacity and performance in children with CP.

8.6 Appendix

Previous collected data to define thresholds

As part of a larger protocol, gait trials at slow and fast self-selected speeds were recorded in addition to spontaneous gait trials in the laboratory. The extremes values within all participants and all groups (CP and TD) were used to define the thresholds.
Minimal time to consider a break in WB, was determined as the maximal time found between 2 strides (most probably during the slow trials)
Aberrant gait cycles were defined from aberrant stride times and shanks sagittal ranges of motion (ROM). Bounds for aberrant stride times were determined from the minimal (most probably during fast trials) and maximal (most probably during slow trials) values of stride time. Similarly, bounds for aberrant shank ROM were determined from the minimal (most probably during slow trials) and maximal (most probably during fast trials) values of stride time. Values are reported in this table:

Table 23 – Thresholds for break and aberrant gait cycles recognition, defined by data recorded in the laboratory

Minimal stride time	**0.6s**		Bounds used for aberrant gait cycle time
Maximal stride time	**4s**	Thresholds used for break definition	
Minimal shank ROM	**25°**		Bounds used for aberrant shank ROM
Maximal shank ROM	**95°**		

8.7 Additionnal results

Associations between the selected gait characteristics and performance quantity measures such as median and maximum number of steps have been performed to complement our analysis and replicate the results found in the literature concerning the link between laboratory-based parameters and performance quantity metrics (Guinet and Desailly, 2017; Mitchell et al., 2015b; Nicholson et al., 2018; Wilson et al., 2015; Wittry et al., 2018) (Table 24). While comparing performance characteristics and performance quantity, no correlation was found except for moderate correlations between the stance duration and the stride length variability with the maximum number of steps. While comparing capacity characteristics and performance quantity, no correlation was mostly found. However, moderate correlations were found for the stride time variability, stance duration variability and the stride length with the maximum number of steps. Besides, two good correlations were found

indicating that the stance phase duration I positively associated with the median number of steps in dialy life, and that the limp is negatively associated with the maximum number of steps in daily life.

Table 24 - Associations between gait function and gait quantity (median and maximal number of consecutive steps) parameters measured in daily life for children with CP

		Median Steps	Max Steps		Median Steps	Max Steps
		DAILY LIFE (Performance quantity)			**DAILY LIFE** (Performance quantity)	
Norm trunk acceleration SD ($m.s^{-2}$)	**DAILY LIFE** (Performance characteristics)	0.43	-0.08	**LABORATORY** (Capacity characteristics)	-0.03	0.32
Cyclogram perimeter/area ratio (-)		0.15	0.08		-0.05	-0.44
Double support (%)		-0.21	-0.40		0.42	-0.47
Stride time (s)		-0.09	-0.15		0.26	-0.23
Stride time SD (s)		-0.30	-0.46		-0.04	-0.63 *
Knee ROM asy index (%)		0.13	-0.13		-0.09	0.23
Knee ROM (°)		0.20	0.04		0.43	0.44
Limp (%)		-0.15	-0.38		0.08	-0.75 **
Shank fractal dimension (-)		-0.19	-0.46		-0.17	-0.50
Speed (m/s)		0.15	0.34		0.11	0.64 *
Stance duration asy index (%)		0.09	0.23		-0.05	0.17
Stance duration (%)		-0.41	-0.56 *		0.68 **	-0.25
Stance duration SD (%)		0.05	-0.29		-0.31	-0.55 *
Stride length (m)		0.12	0.37		0.24	0.56 *
Stride length SD (m)		0.54	0.59 *		0.05	-0.38
Walk ratio ($x10^{-2}$ $m.min.step^{-1}$)		0.11	0.34		0.40	0.22

**: p-value <0.05; **: p-value <0.01; ROM: Range of motion; SD: Standard deviation; Asy: asymmetry*

Total, these results were mostly in accordance with previous studies since the majority of our parameters assessed in the laboratory were not associated with the quantity of walking in daily life. However, we underlined some good correlations which could be relevant axes for further investigations.

Part IV

CONCLUSION

Chapter 9

General discussion and perspectives

Abstract

This final chapter proposes an overall discussion regarding the doctoral work. First, the main contributions of the studies included in this thesis are reported. Then, several methodological and clinical aspects are discussed, linking various chapters with one another. Subsequently, the main limitations are reported, after what some technical and clinical perspectives are presented.

9.1 Summary of main contributions

The main objective of this thesis was to assess gait of children with CP in a daily life context and compare it with gait in the laboratory, to gain more insight regarding the comparison between capacity and performance. For this purpose, two thesis axes were followed. The first was to propose a valid tool for gait assessments in daily life based on existing methods. Although plenty of tools with appropriate computational methods have been developed, only a few of them were designed for clinical comprehensive outcomes assessments in children with CP. Furthermore, most of the systems were not tested in natural conditions. For this technical part, attention was paid to choose a system providing spatiotemporal parameters (STP) with the highest possible level of accuracy, since these gait outcomes were promising clinical features to be accurately assessed in daily life settings. The second axis was to compare gait parameters assessed in, or close to, daily-life conditions with the same gait parameters assessed in the laboratory during standard CGA protocol. This clinical part of the thesis adopted a progressive approach, starting with the comparison between standardized gait and gait under challenging situations (dual tasks) in the laboratory and ending with the actual comparison between standardized gait and gait in real-life settings. The thesis focused on the evaluation of objective, accurate and relevant metrics, similar for both environments.

9.1.1 Wearable system for spatiotemporal parameters (Chapter 4)

To choose an appropriate system for STP estimation in children with CP, a comparison of three relevant existing sensor configurations was undertaken. The requirements were the following:

1) To provide an accurate and precise estimation of the three main STP (stride time, length and velocity) used in the clinic,
2) To be comfortable for long-term monitoring,
3) To be easy-to-use,
4) To allow the computation of other gait features relevant to the CP population.

The first requirement was assessed through a validation protocol, where children wore several sensor configurations as well as reflective markers. Reference STP were thus recorded with the clinical standard (optoelectronic system and force plates) and concurrently STP were computed from the three tested wearable systems. Accuracy and precision were computed for temporal, spatial and spatiotemporal outcomes in the groups of TD children, children with CP with a lower level of impairment and children with CP with a higher level of impairment. This study highlighted variable performances of the systems depending on the sensor configuration and the level of impairment of the children. Indeed, the configuration using sensors on both feet was found more accurate for typical and regular gait patterns, while sensors located on the shanks and thighs performed better for moderate to severely impaired gait patterns. The system using sensors only on the shanks, which computational method relied on optimization based on adult data, was found not suitable for spatial outcome estimation in children. Besides, the main inconvenient of the direct integration method, used with the feet configuration, is that it relies on foot flat instants during midswing of each gait cycle. However, CP gait pattern is often characterized by an absence of foot flat period.

The second, third and fourth requirements were addressed in the discussion section of the study. Comfort assessed by informally questioning the children during the measurements. To be independent of shoe-wearing and allow the monitoring of all gait episodes within a day, feet sensors were fixed directly on the feet, unlike most studies where sensors were fixed on the shoe (Brégou Bourgeois et al., 2014; Dadashi et al., 2013; Hegde et al., 2016). While testing this solution during a semi-standardized sequence outside of the laboratory (with shoes), it proved to be inappropriate for daily life assessment, especially for children wearing Ankle Foot Orthoses (AFO) who complained about the pain while the sensor was compressed between the foot and the orthosis. Even if the shank-and-thigh configuration was more cumbersome, sensors were well supported; they

were worn under the clothes and did not hinder the children's activities. Furthermore, the shank-and-thigh configuration discriminates several postures (sitting, lying, and standing) that the feet configuration could not. Computation of complementary parameters, valuable for the assessment of children with CP, like the foot clearance and foot to floor angles can be computed only with the feet configuration, and the knee angle only with the shank-and-thigh configuration. Combining these practical aspects with the accuracy of the measurements, this study recommended selecting the configuration using sensors on the shanks and thighs for the next steps, i.e. for long-term assessments in laboratory-free conditions.

Overall, the chosen system had these specifications, according to the requirements:

1) 3ms accuracy (72ms precision) for stride time estimation, 7cm accuracy (14cm precision) for stride length estimation and 0.07m/s accuracy (0.12m/s precision) for walking speed estimation, regardless of the impairment. (Stride time ranged between 1.06 and 1.20s, stride length ranged between 0.90 and 1.28m and speed ranged between 0.81 and 1.20m/s in our population.). Table 25 gives an overview of the performance of the system as compared to 2 existing studies.

Table 25 – Comparison of 3 wearable sensor configurations (including ours) regarding the validation measures reported for stride length and stride velocity computation in children with and without CP (against an optoelectronic system)

	(Carcreff et al., 2018)	**(Brégou Bourgeois et al., 2014)**	**(Mackey et al., 2008)**
Sensor configuration	shanks, thighs	feet	feet, legs, trunk
Populations description	15 CP - GMFCS I-III; 11 TD	14 CP - GMFCS I,II; 15 TD	25 CP - GMFCS I-III; 30 TD
Mean age (years)	13	11	14
Stride length (m)			
Mean difference	0.045	0.036	0.440
Limit of agreement	0.183	0.090	0.370
Stride velocity (m/s)			
Mean difference	0.036	0.055	0.185
Limit of agreement	0.166	0.082	0.430

2) Adequate fixation (PALStickies, PAL Technologies, Glasgow, UK) which provided satisfactory sensor support and comfort for the participant was defined for long-term measurement (3 days, 10h/day).
3) Easy to use sensors (Physilog 4, GaitUp, Renens, Switzerland) for non-experts with fast charging, a single start/stop button and informative LEDs.
4) Detection of lying, sitting and standing postures.
5) Computation of the shank, thigh and knee angles and the smoothness of the shank and thigh movements.
6) Distinction between right and left sides, i.e. between the paretic and non-paretic sides when relevant.

The main contribution of this study was to test three wearable systems and for a population of children including those with a high level of CP (until GMFCS III). Indeed, children with a higher level of impairment are crucial to consider since they may benefit even more from the assessment of their gait performance. This work has also permitted to emphasize the importance of sensor location and biomechanical assumptions for parameters computation when dealing with CP. Since gait patterns can be highly atypical, assumptions based on adults' or TD children's gaits do not necessarily suit children with CP.

9.1.2 Personalized approach for walking bout detection (Chapter 5)

To evaluate gait parameters in daily life settings, specific walking bout detection is required. Performances of methods using fixed thresholds for signal features recognition (like the one proposed by Salarian et al. (2004)) tend to decrease when the tested gait patterns are unusual such as slow and/or impaired walking (Bertuletti et al., 2019; Muñoz-Organero et al., 2017; Sanjay K. Prajapati et al., 2011) like in children with CP, and also when they are tested in different settings (Pham et al., 2017; Sessa et al., 2015) and footwear (Anwary et al., 2018a). Alternative approaches were then considered to provide a high level of walking bout detection specificity. Conventional machine learning approaches were excluded since the required high amount of data to train the model was not available.

Given that children with CP regularly visit their clinicians (during what they are asked to walk along a short path in the consultation room for a qualitative observation at least), the idea was to collect information about the children's gait pattern during these visits to customized thresholds for walking bout detection in natural settings.

A CGA protocol followed by a semi-standardized protocol outside of the laboratory and in the hospital surroundings was set. A sub-set of participants, presenting heterogeneous levels of impairment, were included in this study to test this alternative walking bout detection approach. Two customized methods and the original method using fixed thresholds were compared on the basis of sensitivity, specificity, accuracy, and precision in walking bout detection with regard to a video recording reference during the semi-standardized route. One customized method used thresholds set for the populations (CP or TD separately), the other used thresholds set for each individual. The findings were that population-based customization improved walking bout detection as compared to the original method and that an individual-based personalization improved it even more, especially with better performance in the detection of true negatives. A certain clinical impact of such an improvement was demonstrated since the walking speed distribution over a 20-minutes sequence of daily-life-like activities was found slightly changed: the minimal walking speeds detected increased with the personalized method. The explanation came from the higher specificity of the method. Indeed, thanks to adjusted thresholds, non-expected cyclical activities performed in real life such as playing on swings were more likely excluded. This alternative gait detection method was thus beneficial, not only for patients but for all the participants. Hence, the individual-based personnalisation was applied in the following clinical studies (Chapters 7 & 8).

> The main contribution of this study was the preliminary investigation of a personalized approach for gait detection in children with CP. Given inherent inter-individual heterogeneity, the personalization of any data processing may be beneficial. Furthermore, this personalized approach can be adapted for multiple purposes and multiple populations.

9.1.3 Standardized gait in laboratory versus gait under dual tasks (Chapter 6)

To begin with the investigations regarding the comparison between gait in laboratory and gait in daily life, a transitional protocol was set, including the evaluation of gait in the laboratory under challenging, reflecting ecological situations. Study participants were exposed to cognitive-motor interferences induced by dual task walking. Walking under dual task is indeed thought to be more representative of daily life walking than traditional CGA protocols, since cognitive demands constantly arise in real-life situations (physical obstacle, people talking, street indications, etc.). When increasing the difficulty of the cognitive tasks, we found that gait abilities decreased, i.e. walking speed, heel clearance and hip range of motion decreased and walk ratio, stride time and stride length variability increased. These observations were not more pronounced for children

with CP than with TD, since the dual task costs (DTCs) were not higher. However, children with CP did have poorer capacities in simple task, so they were actually more penalized during dual tasks.

Although this study confirmed the negative effects of dual task while walking in both populations, the main contributions of this study as compared to existing literature were the findings that DTCs were comparable in children with and without CP. Interestingly, the same conclusions were drawn later on (November 2019) by another research group (Palluel et al., 2019). This brought new hypotheses for the underlying mechanism of cognitive-motor interferences in children. Children with TD may saturate equally their baseline brain resources during dual tasks. Moreover, the added value of this study was the diversity of outcomes measured during dual tasks. Not only STP parameters but also kinematics was impacted by the dual tasks.

9.1.4 Standardized gait in laboratory versus gait in daily life (Chapters 7 & 8)

The two last chapters were devoted to the direct comparison between gait assessed in the laboratory and gait assessed in daily life. The first study intended to understand how fast the children with CP and TD walk in their daily life as compared to what they show to the clinicians or investigators during clinical assessments. Using the wearable devices and associated algorithms previously chosen (Chapter 4), walking speed distribution throughout 3 days was computed. Although at the individual level, children with CP showed heterogeneous behaviours, at the group level, they showed a lower walking speed in daily life as compared to the laboratory. Furthermore, a positive high correlation was found between speeds in the laboratory and daily life for children with CP. Neither significant difference nor correlation was found for children with TD.
The second study focused only on the daily-life walking bouts with a traveled distance equal to the laboratory walkway length, to compare more equivalent walking contexts. Sixteen parameters, belonging to several gait domains, were computed and compared. Most of the gait parameters of children with CP were highly correlated between both environments and the significant differences found were in the way that capacity exceeded performance. However, these observations were not as obvious and significant for children with TD. Additionally, weak associations were found between parameters of the gait function assessed in daily life and indicators of gait quantity like the median and the maximal number of consecutive steps in daily life, which was more in line with previous literature.

The main contribution of these studies as compared to previous research was the selection of objective and identical metrics to compare gait in the laboratory, related to *capacity*, and gait in daily life, related to *performance*. Contrary to recent literature, high correlations were highlighted in children with CP between capacity and performance. The findings indicated that the gait function assessed in the laboratory was a good indicator of the gait function in real life for children with CP. As compared to children with CP, children with TD seemed to be more able to adapt their gait to the context as no such correlation was found. Furthermore, the added value of these studies was the number and the nature of the gait outcomes. To the candidate's knowledge, no existing study has assessed gait *performance* on the base of spatial, spatiotemporal and angular parameters, and no existing study has selected the daily life WB according to the traveled distance.
In addition to scientific contributions, these studies had the merit to be the first to evaluate gait function characteristics in the children's daily life. They have thus brought useful practical information on the feasibility of such assessments for future similar protocols.

9.2 Discussion

9.2.1 Wearable system for gait analysis in children with CP

9.2.1.1 Challenge using inertial sensors in CP

CP describes a heterogeneous population characterized by motor disorders affecting variable body parts and with variable intensities. Children with CP demonstrate thus atypical and variable gait patterns. Even if some classical patterns have been described in the literature, such as crouch gait, jump knee or true equinus (Papageorgiou et al., 2019; Rodda and Graham, 2001; Rodda et al., 2004), mixed and atypical disorders can be found, resulting in unique ways of walking. This is why the assessment of gait with inertial sensors in children with CP constitutes a major challenge. Indeed, using IMUs for gait analysis entails making generalizations about expected features to detect (Fasel, 2017). For instance, during gait we expect that the supporting leg is fully extended during mid-stance so this property can be used to cut the gait cycle. IMUs measure physical quantity in the local coordinate frame and have the particularity to be subject to drift when position, speed or orientation are targeted (Kluge et al., 2017). Biomechanical assumptions, based on the specificity of the monitored activity and population are generally exploited to determine the sensor frame's orientation with respect to the body segment's frame, and to overcome the drift issue (Fasel, 2017). This has been highlighted in the first study of this thesis (Chapter 4). The common assumption of foot-flat during stance, used as 'motionless' instants for the initialization of acceleration integration (Mariani et al., 2010), is not achieved by nearly 50% of the CP cases, according to Rodda et al. (2004). Similarly, active or passive limbs movements used in several methods to align the sensor frame with the body segment's frame, called 'functional calibration' (Favre et al., 2009), cannot be well achieved by nearly all the patients with CP since they practically all have joint contractures or bone deformities (Gage et al., 2009), preventing from reaching full extension of certain joints. New and individualized rules need to be determined for gait analysis in CP. Indeed, the heterogeneous characteristic of CP leads to personalized, patient-tailored approaches. This idea was succinctly developed in the second study of this thesis (Chapter 5) and revealed to be relevant. Further works in this direction are recommended.

9.2.1.2 Sensor configuration: compromises between accuracy, inconvenience, and relevance

For daily life monitoring, the idea is to record motion in the long term. Therefore, on one hand, the wearable system has to be the least disturbing for the patient (small sensors, low number of sensors, light and painless fixation, high autonomy, etc.). On the other hand, the system should allow detecting diverse activities and posture in order to allow drawing a true picture of the subject's panel of activities within a day. Similarly, for motion capture, systems allowing the measurement of a higher number of features for the computation of comprehensible and relevant outcomes confer a substantial advantage for gait analysis (Attal et al., 2015; Paraschiv-Ionescu et al., 2012). Obviously, increasing the number of sensors lowers the comfort for the participant but strengthens the performance of the algorithms and increases the number of additional outcomes and features detectable. A smart compromise needs then to be found between accuracy, the number of outcomes and inconvenience for the patient. The choice of the most appropriate wearable system (Chapter 4) was indeed made in accordance with this compromise.

A single trunk sensor configuration was further proposed by our research team for walking bout and cadence detection in children with CP and TD (Anisoara Paraschiv-Ionescu et al., 2019). Despite its higher convenience and the overall good accuracy (up to 2%) and precision (up to 9%) for cadence estimation, this sensor configuration permitted only the detection of a single temporal parameter. Further work is indeed necessary to increase the potential of single-senor configurations.

A compromise between the accuracy of the system and the clinical relevance of the assessment is to be found too. The study in chapter 4 has also emphasized a decrease of algorithm performances with regard to the level of impairment of the child. However, children with a higher level of impairment, i.e. who walk very slowly with small steps, constitute the target population of high interest for measurement of community-based walking in order to plan an intervention (Bjornson, 2019).
Universal recommendations cannot be suggested. Every clinical application should drive its choice of sensor configuration (Del Din et al., 2016c), sensor fixation and expected performance.

9.2.1.3 Clinical meaning of wearable's outcomes

Clinicians and therapists are interested in knowing more about how their patients behave outside of the clinic. Investigations were only carried out through questionnaires until the advent of technological solutions which provided objective outcomes. Pedometers and accelerometers, which detect impacts during locomotion, were extensively used in clinical research to evaluate physical activity (Yang and Hsu, 2010). The majority of existing literature on the use of wearable devices in children with CP concerned pedometers and accelerometers with limited outcomes like the number of steps, intensity, and frequency of physical activity (section 1.3.3.3, Chapter 1, (Hsu et al., 2018)). A well known and highly-used commercial accelerometer (Actigraph, USA) converts the magnitude of acceleration into 'activity counts' representing the estimated intensity of activity during a period of time (called epoch). Although activity counts appear, at first, very simple to understand for non-experienced users, their computation relies on empirical thresholds, which makes difficult the comparison between studies (Banda et al., 2016). Furthermore, researchers and clinicians using such accessible devices can be confused. Bjornson K. (2019) has pointed out that some can mix physical activity and walking. Similarly, according to Palisano R.J. (2012), authors may give inappropriate recommendations to increase physical activity by increasing their total daily number of steps whereas joint protection has to be considered for some patients like those with CP. Physical and clinical meanings of wearable's outcomes need to be considered intelligently to take the best advantage of them.
In this thesis, we chose to compute CGA-like parameters, i.e. reflecting gait characteristics, so that there will be higher chances to be understood and properly used by the clinicians.
Several studies took advantage of acceleration and angular velocity raw data to compute some clinical indexes (Chen et al., 2017; Menz et al., 2003; Rueterbories et al., 2013). The movement smoothness is also commonly studied with IMU data (Brach et al., 2011; Chen et al., 2017; Menz et al., 2003; Newman et al., 2017) and we actually computed it in the last study of this thesis. It revealed to be a discriminative parameter between children with CP and with TD, since very good correlation was found between the laboratory and the real life in children with CP but no correlation in children with TD. The principal drawback of these new parameters is the lack of representativeness. The collection of a high amount of data from healthy participants is then needed to set normative values in order to help the understanding of the index or the new metric. Such parameters, that are unusual in clinical practices today, could constitute tomorrow's common gait parameters.
To conclude, IMUs can provide many outcomes possibilities and offer new pieces of information about patients' gait or physical activity that are relevant for clinicians. However, it is necessary to work on data presentation for clinical considerations.

9.2.1.4 Wearable's validity for clinical purposes

Very affordable mainstream gadgets like fitness trackers or pedometer application for smartphones, have overwhelmed the market over the past few years and still continue (Shin et al., 2019). Shin et al. reported that the overall market of commercial wearable activity trackers, such as Fitbit (Fitbit inc., USA), Xiaomi (Xiaomi inc, China) and Apple Watch (Apple, USA) is expected to grow from 113.2 million units sold in 2017, to 222.3 million in 2021, according to the International Data Corporation Worldwide Quarterly Wearable Device (Shin

et al., 2019). Beyond the mainstream use, such consumer wearable pieces of equipment and mobile applications are of high interest for clinical applications. However, the drawback of this new fashion phenomenon is that devices are developed but are rarely validated against a gold standard (only 5% formally validated (Peake et al., 2018)). For instance, the accuracy of step counting of one of the most popular fitness trackers (Fitbit Flex, USA) was assessed on healthy adults in controlled and free-living settings (Feehan et al., 2018). Accurate measures (i.e. within ±3% for the laboratory conditions and within ±10% for the free-living conditions) were provided by the device only in 50% of the cases. While certain users of such commercial device can show a poor interest in device accuracy (Shin et al., 2019), clinicians certainly seek for the most accurate devices. Their validity (accuracy, precision, repeatability) needs to be carefully considered for clinical applications such as gait analysis in children with impairment, from what therapeutic decisions can arise. One can observe that the results found regarding the difference between spatiotemporal parameters assessed in the laboratory and the daily life (Chapter 8) were borderline with our system's precision. This is typically crucial information to give to the clinicians before any interpretation of the results any the case of a real clinical application.

9.2.1.5 Challenges related to measures in daily life

Measurements in daily life, i.e. real-world situations, are by essence not controlled which constitutes the major advantage from a clinical point of view but also the major drawback from a methodological point of view (Del Din et al., 2016a). Several aspects of real-world assessments were addressed in this doctoral work concerning the methodological feasibility. Apart from the sensor configuration which is more specific to the population and the application (section 9.2.1.2), sensor fixation, sensor autonomy, and easiness of use are crucial criteria for the success of any real-life measurements. The sensor fixation determines the convenience to wear the sensors and the consistency of the recordings, e.g. if the sensor fixation is not appropriate, the sensor can fall off obliging the participant to relocate it. A large proportion of studies used an elastic belt to fix a sensor located at the lower back (Van Ancum et al., 2019) but relative displacements of the sensor with regard to the body is expected with such a system. The main solutions reported in the literature for other sensor configurations are adhesive tape, surgical tape, elastic straps or Velcro straps which prevent from relative movements (Fong and Chan, 2010). We opted for a double-sided hydrogel (PALsticky, PALtechnology) which conferred the substantial advantage to be pain-free and re-usable. This solution was adopted by other research groups (Del Din et al., 2016c, 2016b; Morris et al., 2017; Tang et al., 2013), covered with an additional adhesive film. However, wearing adhesive tape or sticky for about a week of measurement may cause skin irritations (Stanton et al., 2014) especially for patients who suffer from hyper-sensibilities like children with CP. This is why Elastane sleeves were designed for protection to avoid using an additional adhesive tape but several participants reported that one sensor fell or was about to fall. Quite a few cases (27%) were concerned by this issue. Thus, the perfect sensor fixation is still to be found to ease as much as possible patient's long term monitoring. The sensor battery autonomy determines the number of times that the participant needs to handle the sensors (turning off, charging, changing fixation, turning on, etc.). It can be considered that the less the participant has to touch the sensor, the better. For this purpose, single accelerometer located at the lower back shows to be the best option, if the battery can last about a week or more (Del Din et al., 2016a; Morris et al., 2017; Supratak et al., 2018; Van Ancum et al., 2019). In our case, the sensor autonomy was around 10 to 15 hours due to the enabled gyroscope, the sampling frequency set at 100Hz and the synchronization between sensors. Families had to take care of sensor recharging and repositioning everyday day, increasing the risk of technical problems. Lastly, the easiness of use determines the amount of missing data. If the sensors are difficult to turn on and off, there is more chance that at least one sensor does not record properly. In this doctoral project, 3.6% of the data were concerned about this issue. A compromise has to be found also between comfort and consistency of the recordings.

9.2.1.6 Knowledge of the context

Another aspect addressed in this thesis related to the challenge of daily life measures is the absence of knowledge of the context of walking. Indeed, while monitoring a patient in his daily life, information about the context of walking is not available as this is difficult to obtain unless using an additional system such as a GPS (Wang and Adamczyk, 2019) or an embedded camera (Hickey et al., 2017a). The use of such additional devices is however problematic due to privacy issue, especially in children. To minimize the lack of knowledge of the context, various solutions have been proposed. First, a minimal number of steps per walking bout is usually set to avoid the inclusion of non-purposeful walking (Del Din et al., 2016c; Hickey et al., 2017b). However, such minimal threshold is difficult to define. Several approaches proposed in the literature relied on the inclusion of prolonged walking bouts (>60 seconds for instance) to capture steady-state walking (Del Din et al., 2016b; Hickey et al., 2017b). However, it has been demonstrated that short walking bouts constitute the majority of ambulatory activities (Orendurff et al., 2008). Especially in pathological populations such as children with CP who have very limited walking abilities, e.g. who cannot walk more than 20 steps in a row, it is not relevant to apply this cut-off. In our study (Chapter 7), we chose to include walking bouts longer than 10 steps and took the whole gait characteristic distribution into account. In addition, inclined and curved paths can be detected with appropriate machine learning techniques (Aminian et al., 1995a) and 3D sensor alignement (Mariani et al., 2010) using the different IMU modalities. Finally, multimodal devices (e.g., Global Navigation Satellite System (GNSS), barometric pressure, microphone, weather records, etc.) could be considered for more information regarding the contexts (Wang and Adamczyk, 2019). This is discussed in the following perspectives section (9.4.1.4).

9.2.2 Gait in laboratory versus daily life

9.2.2.1 ICF model

The ICF model (World Health Organization, 2002) was initially set to move the focus from the pragmatic impairments of individuals with a disability to the impact of their impairments on their personal and social aspects (Fauconnier et al., 2009).

Functions, activity and participation

The ICF proposed reciprocal relations between body structures and functions, activity, participation (involvement in a life situation), and personal and external environmental factors (Bjornson et al., 2013) as described in the introduction of this thesis (section 1.3.2.1). However, those relations may not be equally balanced. Fauconnier et al. have shown with a cohort of 818 children with CP across Europe, that gross and fine motor disorders, intellectual disability, communication issues, and pain were significantly associated with lower participation, whereas sociodemographic, i.e. external and personal factors were not (Fauconnier et al., 2009). In fact, activity is at the center of the latest definition of CP (Bjornson et al., 2013; Rosenbaum and Dan, 2019): "*a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain.*" (Bax et al., 2005). Activity and participation are tightly interlinked. However, capacity (what the individual can do in a standardized environment) and performance (what an individual does in his actual environment), which are both qualifiers of activity, may not act equally on participation. Bjornson et al. have indeed demonstrated that the relation between capacity and the overall frequency and diversity of participation, assessed through questionnaires, is mediated by the performance (Bjornson et al., 2013). Ultimately, regardless of the motor functions and activity limitations, participation is at the forefront of clinicians' and therapists' concerns (Bjornson et al., 2013) since it is associated with well being (Omura et al., 2018). This is why performance assessment have gained that much interest.

Proposition of an adapted ICF model fitting the walking activity in children with CP

This thesis aimed to integrate ICF concepts to try better understanding the discrepancy between both constructs of activity: capacity and performance. We tried to propose an adaptation of the ICF components to the CP condition integrating the notions previously discussed (Figure 54).

The 'Body Function and Structure' of interest is thus the 'gait pattern function' (b770) defined in the ICF as "Functions of movement patterns associated with walking" (Schiariti, 2014) appertaining to the 'Neuromusculoskeletal and movement-related functions' (b7) (Schiariti et al., 2014b). The gait pattern function is recruited for the 'walking' (d450) activity defined as "Moving along a surface on foot, step by step, so that one foot is always on the ground" (Schiariti, 2014). Walking has been divided into gait capacity and performance, as suggested by the ICF. To complement this model we divided them into 'characteristics' and 'quantity', which can be associated with the recently proposed terminologies 'micro' and 'macro' structure of gait (where 'micro' structure refers to discrete gait characteristics contained in walking bouts and 'macro' structure refers to the volume, i.e. the quantity of gait) (McArdle et al., 2018). In our proposed terminology, gait capacity quantity refers to walking endurance in a standardized environment (e.g. under the instruction to "walk as long as possible" or during the 6MWT (Maher et al., 2008)). This aspect was not evaluated in this thesis, but was found poorly associated with gait capacity characteristics (assessed through GDI) in some studies (Maanum et al., 2012; Wilson et al., 2015). Gait performance quantity refers to the amount of ambulatory activity detected in the children's daily life (e.g. step count) and was found not associated to gait performance characteristics, with the exception of few moderate correlations (additional results in Chapter 8). The study in chapter 8 has pointed out that gait characteristics measured in clinical conditions, which constitute the current standard condition for gait evaluation in CP, are highly associated with the gait characteristics in daily life. This was not verified previously in the literature when comparing gait characteristics in the laboratory with gait quantity in daily life (Guinet and Desailly, 2017; Nicholson et al., 2018; Wilson et al., 2015). Figure 54 illustrates this adapted model of the ICF highlighting the associations found in previous studies and in the current doctoral studies. The generic scheme of the ICF is provided in Chapter 1, page 16.

Given the set-up used in this thesis, further relevant work could be now to determine the predictors of the gait performance quantity or characteristics that can be measured in the laboratory (i.e. gait capacity predictors).

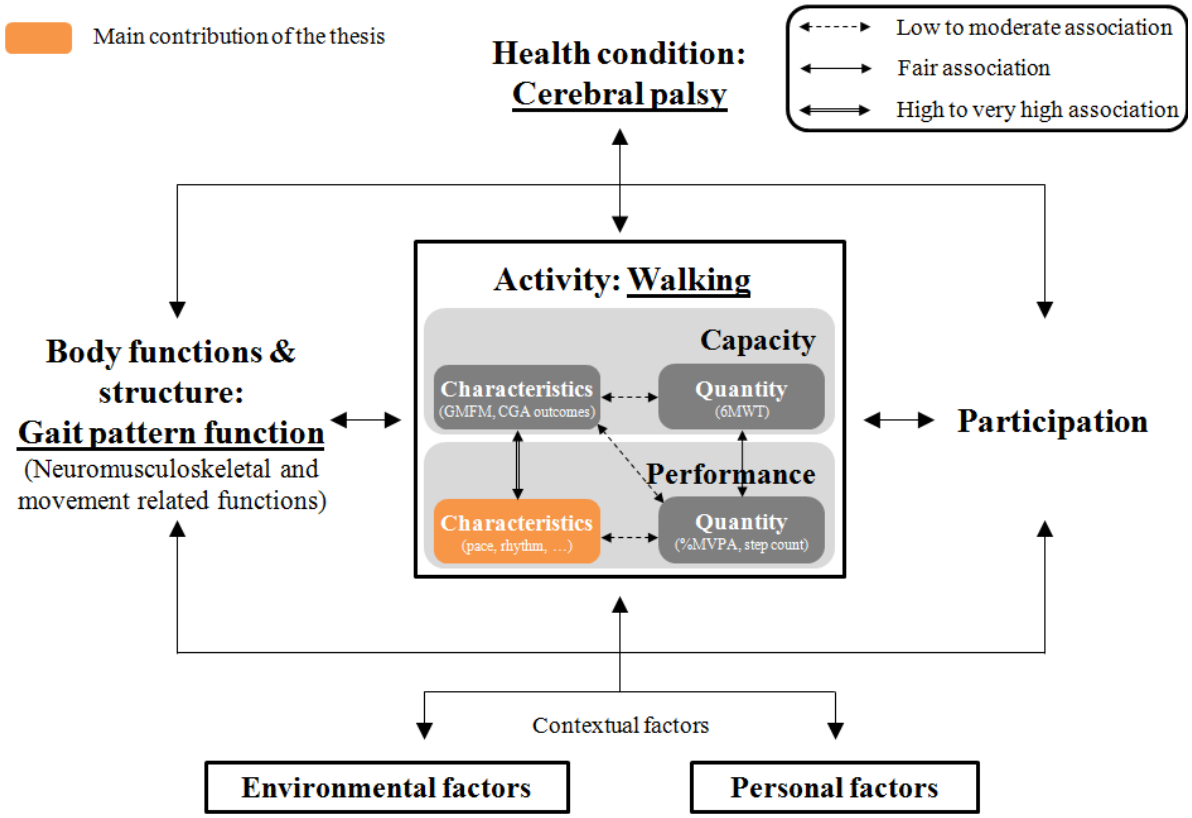


Figure 54 – ICF model applied to cerebral palsy and gait in the laboratory (capacity) versus daily life (performance)

This adapted ICF model reflects the complexity of inter-relations between the different components of the walking activity.

9.2.2.2 Bridging the gap

Traditionally, children with CP are evaluated in clinical settings to help clinicians to have a thorough understanding of the clinical picture and to distinguish between the primary, secondary and tertiary impairments. We have broached the idea that other gait assessments could help even better understanding the child's difficulties, including contextual factors as suggested by the ICF model (Figure 54). Two protocols were advised for this purpose: the dual-task and the daily-life protocols. In agreement with a recent study (Hillel et al., 2019), our dual-task protocol was sought to be a step toward better understanding the gap between gait in the laboratory and gait in the daily life. Hillel et al. found that dual-task walking parameters of 150 elderly participants were generally closer to the values obtained during daily life walking (Hillel et al., 2019). As an attempt to make the same comparison for our population of children with CP, Table 26 reports gait performance characteristics evaluated during our two protocols as compared to gait capacity characteristics assessed in the laboratory under spontaneous and self-selected gait. The values are taken from the study conducted for Chapter 6 (the dual task 'Animals' was taken as an example to represent the average difficulty) and the study conducted for Chapter 8. The children assessed in these two studies were different, especially regarding the GMFCS levels (in the dual task protocol, only children with CP with GMFCS I and II were included), so this table allows making only a rough comparison of the average of the common parameters evaluated.

Table 26 – Group averages of gait characteristics (walking speed, stride time and walk ratio) assessed during spontaneous walking, walking under dual-task in the laboratory and walking during daily-life

		CGA[1]	**Dual task**[2] (*Animals*)	**Real life**[1]
Walking speed (m/s)	CP	1.15 [0.84-1.27]	0.66 [0.50-0.86] ◄►	0.91 [0.65-1.01]
	TD	1.28 [1.18-1.38]	0.85 [0.76-0.96] ◄►	1.15 [1.11-1.19]
Stride Time (s)	CP	1.03 [0.98-1.18]	1.31 [1.15-1.44] ◄►	1.25 [1.18-1.32]
	TD	1.07 [0.98-1.12]	1.24 [1.13-1.45] ◄►	1.12 [1.08-1.21]
Walk ratio ($x10^{-2}$ m.min.step^{-1})	CP	1.01 [0.88-1.19] ◄►	0.56 [0.50-0.64]	1.10 [0.94-1.17]
	TD	1.23 [1.10-1.31]	0.66 [0.55-0.76] ◄►	1.13 [1.00-1.29]

[1]: (Participants from Chapter 8) CP group: n=14, age: 12.6 [11.4:13.9] years, 6 GMFCS I, 3 GMFCS II, 5 GMFCS III; TD group: n=14, age: 12.3 [11.5:14.5] years

[2]: (Participants from Chapter 6) CP group: n=18, age: 12 [10:13] years, 16 GMFCS I, 2 GMFCS II; TD group: n=19, age: 12 [10:13.5] years

In each condition, the measured walking distance was approximately 10m. The double-sided arrow indicates the closest values between the dual task walking and the two other conditions.

One can observe that spontaneous walking, dual-task walking, and real-life walking differed indeed. Unexpectedly, the decline of gait characteristics was more pronounced in dual task than in real life. Except for the walk ratio, the dual task appeared thus to be the most challenging condition for gait in both groups (decreased speed and increased stride time). This suggested that the applied cognitive load during the categorical fluency task, like 'Animals', may have been higher than during usual walking in daily life on short distances. Actually, this was in accordance with Hillel et al.'s results with elderly people, different cognitive tasks and longer walking bouts (30 seconds).

On a technical point of view, it is interesting to note that the differences between spontaneous and dual-task walking in standardized settings were much higher than our wearable system's precision (x4 for stride time and walking speed approximately) which imply that our wearable system could be used to detect dual-task effects in patients with CP.

What can be remembered is that dual task may explain part of the real-life walking, but not all of it. More disturbing factors play a role in gait performances like the environment, motivation, mood, or fatigue which were not evaluated in the framework of this thesis. Further work is needed to investigate the mediating effects of those factors.

9.2.2.3 Considerations for assessment

Since gait capacity was found associated with the performance; capacity exceeding performance in CP, performance assessment should not necessarily provide more information than traditional CGA. However, given the high heterogeneity of the CP population, precise estimation of locomotion performance cannot be given on the base of gait capacity. Indeed, for instance, higher inter-subject variability was found within the CP group regarding dual task costs (DTC), as compared to healthy controls (Chapter 6, (Carcreff et al., 2019a)). Similarly, the difference of walking speed, and other gait parameters related to the gait function, between laboratory and daily life assessments was more variable across subjects with CP than with TD (Chapters 7 and 8). This has favored the strength of the associations.

Future clinical evaluations should thus integrate dual task assessments, in order to better reflect, or even exaggerate the effect of cognitive-motor interferences on the gait performances which occurs in daily life (cf. preceding section 9.2.2.2 mentioning worst results in dual task as compared to the daily life). Furthermore, clinical evaluations should include performance assessments as a complement to CGA data to gain objective

information on the gait function in the actual real life of the patient. This has been recently highlithed in a recent review published in the Lancet Neurology (Warmerdam et al., 2020), where it is stated that data collected in ecological environnements can indeed help capture long term, fluctuating or rare occurring events which have the high potential to support clinical decision making. The authors of this review proposed a comparison of various parameters related to gait and posture between the supervised and unsupervised environments in the elderly population, and pathological populations of patients with PD and Multiple Sclerosis. In accordance with our results in children with CP, substantial differences were found (Warmerdam et al., 2020).

For now, wearable systems present several limitations that preclude to measure as many gait parameters and as accurate as in laboratory settings. Therefore, performance assessment, i.e. the assessment of the gait function in a natural environment, and laboratory-based assessment like CGA complement one another. Integrating ecological protocols into the clinical routine should then be advised in addition to CGA.

The evaluation of surgery outcomes through the measure of quantity of walking activity was proposed by Nicholson et al. (2018), but they found weak correlations between the change in gait capacity characteristics (assessed by the GDI) and the change in gait performance quantity (daily number of strides). We suggest that surgery outcomes, as well as the outcomes from other type of interventions, such as intensive physiotherapy, electrostimulation, medication or orthosis, could also be explored in daily life through gait characteristics evaluation.

9.2.2.4 Considerations for interventions

Traditionally, clinicians focused on body functions and structures reinforcement in clinical settings and assumed that the benefits will be transferred to real life. Our findings indeed suggested that gait function disorders can be trained or corrected in standardized settings to help the child to improve his gait function in daily life. But we have also highlighted the gap between activity constructs, capacity and performance. More and more therapeutic programs aim at minimizing this gap, which means finding strategies allowing children to fully exploit their capacity in daily life.

Dual-task protocols have great potential for this purpose. Benefits of dual-task training have indeed recently been demonstrated in several populations (Conradsson and Halvarsson, 2019; Liu et al., 2017; Wollesen et al., 2017; Yang et al., 2019), and also in children with unilateral CP (Elhinidi et al., 2016). The training protocol proposed by Wollesen et al. (2017) draws particular attention since it is very detailed and complete. It consisted of two phases with increasing difficulty, during which patients were asked to perform tasks in conditions mimicking those of daily living. Meanwhile, the investigator provided strategies to deal with the disturbances. This kind of program could indeed constitute a very relevant training for children with CP who experience great difficulties dealing with cognitive-motor interferences.

Furthermore, performance-based training at home can be considered. Home-based training has already been tested and has shown good results to improve upper-body function (Hung et al., 2018; Lorentzen et al., 2015), balance (Katz-Leurer et al., 2009), walking abilities and daily activities (Bilde et al., 2011; Lorentzen et al., 2015) in children with CP. Indeed, this improvement can be due, on one hand, to the child and the family's responsibility-taking in the training process while doing exercises at home (Bilde et al., 2011; Hung et al., 2018) and on the other hand, to the time extension of training as compared to physiotherapy sessions only (Bilde et al., 2011). Furthermore, these therapies are 'task-oriented'; hence they allow the child training in practical and realistic situations. A fair analogy with sport training was proposed by Bjornson K. (Bjornson et al., 2013). Although stationary exercises, treadmill sessions and weight workouts are necessary for the athlete's preparation, the actual practice of the activity in a real environment (e.g. road, swimming pool or snow tracks) is essential to achieve the best outcomes during competitions (Bjornson et al., 2013). Likewise, tracking gait function in daily-life settings ensures that the effects of a treatment or a therapy ultimately generalize into daily

settings. The main drawback of home-based rehabilitation and training is the decrease of motivation with time (Lorentzen et al., 2015). Several strategies to maintain the child's motivation have been proposed, like internet-based exercises (Bilde et al., 2011; Lorentzen et al., 2015). Wearing IMUs could be a solution for portable, accurate and cost efficient body tracking, and could constitute a great source of motivation for the children, especially if some serious games can be associated to it (Tannous et al., 2016).
In summary, to exploit capacity at best, the child needs to bring exercises home and train on a daily basis. This suggests that interventions should focus on what the child is used to do in his real life to improve performance (Bjornson et al., 2013). Indeed, performance assessment is clearly in the perspective of tailored intervention programs, in order to have better and longer results. The use of IMUs has the potential to guide therapists in setting such personalized intervention programs.

9.3 Limitations

These thesis contributions have to be considered in light of their limitations which have been discussed for each study in the respective chapters. Nevertheless, several global or recurrent limitations, and trails for improvement can be reformulated here.

9.3.1 Regarding the study participants

As reported for each study, the main limitation was the sample size. Given the heterogeneity of the CP population, this limitation was critical. The sample size was however calculated at the initiation of the projects in order to suit the research questions. For studies in chapters 4, 7 and 8, sample size aimed to suit averages comparison of children with CP and TD based on previous data using wearable sensors (Brégou Bourgeois et al., 2014). Sample sizes of 5 participants per group were computed. Hence, in order to obtain a representation of all levels of motor impairment throughout GMFCS I-III, 5 children with CP of each level (15 in total) were elected and 15 controls. In the end, 16 children with CP (7 GMFCS I, 3 GMFCS II and 6 GMFCS III) and 15 children with TD were recruited. Due to one withdrawal (TD) and one exclusion (CP), 15 children with CP (6 GMFCS I, 3 GMFCS II and 6 GMFCS III) and 14 children with TD were effectively included in the analysis. The imbalanced repartition across GMFCS levels was due to the patients' characteristics in the Geneva area. Indeed, patients with CP were recruited from one site, Geneva University Hospitals (HUG), which limited the number of eligible participants.
For the study presented in Chapter 6 (dual tasks), the sample size was computed to suit average comparison of the walking speed between simple and dual tasks based on previous data in CP (Katz-Leurer et al., 2014). The sample size of 6 participants per group was initially computed, and to obtain a representation of all levels of motor impairment throughout GMFCS I-III, we elected a sample of 18 children with CP plus 2 children for security. In the end, 20 children with CP (16 GMFCS I, 2 GMFCS II, 1 GMFCS III and 1 GMFCS IV) and 20 children with TD were effectively recruited for this study. Due to an even greater imbalanced repartition across GMFCS levels, we decided to analyze only children with GMFCS levels I and II, i.e. 18 children with CP (16 GMFCS I and 2 GMFCS II). One TD participant was an extreme outlier and was excluded from the analysis.
'Extra' inclusions (to compensate the exclusions) were not feasible due to recruitment difficulties. Indeed, despite a 30 to 50CHF shop voucher was given to each participant, about 30% of the eligible participants did not agree to integrate or to complete the study they were included in. Considering that 2 hours were needed for each protocol, the main reasons were the child's and/or parents' unavailability or unwillingness, especially for children who were already busy on a weekly basis with school and medical appointments (physiotherapist, logopedist, etc.). To increase the sample size, a multisite study needs to be carried out.
The difficulty in scoring the GMFCS level has to be mentioned. Level descriptions are not very precise (Palisano et al., 1997) which implies that in some cases, a child can belong to two level descriptions. This can

be a reason for such an imbalanced repartition of children across the GMFCS levels, especially the small GMFCS level II representation, as compared to other studies (Schwartz and Munger, 2018).
Low sample sizes obliged to perform non-parametric tests, which limited the statistical power of the analyses. It should be noticed that the effect size, which does not depend on sample size, was reported when possible in addition to p-values (Sullivan and Feinn, 2012). The validity of the PCA approach proposed in Chapter 6 for the selection of our variables may have also been limited due the low sample size.
In addition, our cohort was heterogeneous in terms of age. Children and adolescents were between 8 and 20 years old. Motor and cognitive functions present turning points in this period of development (Olivier et al., 2010). In Chapter 6, we have indeed observed that younger children (with or without CP) presented higher DTCs than older children. However, the lower sample size of the other studies of this thesis did not allow performing investigations on subgroups of age.

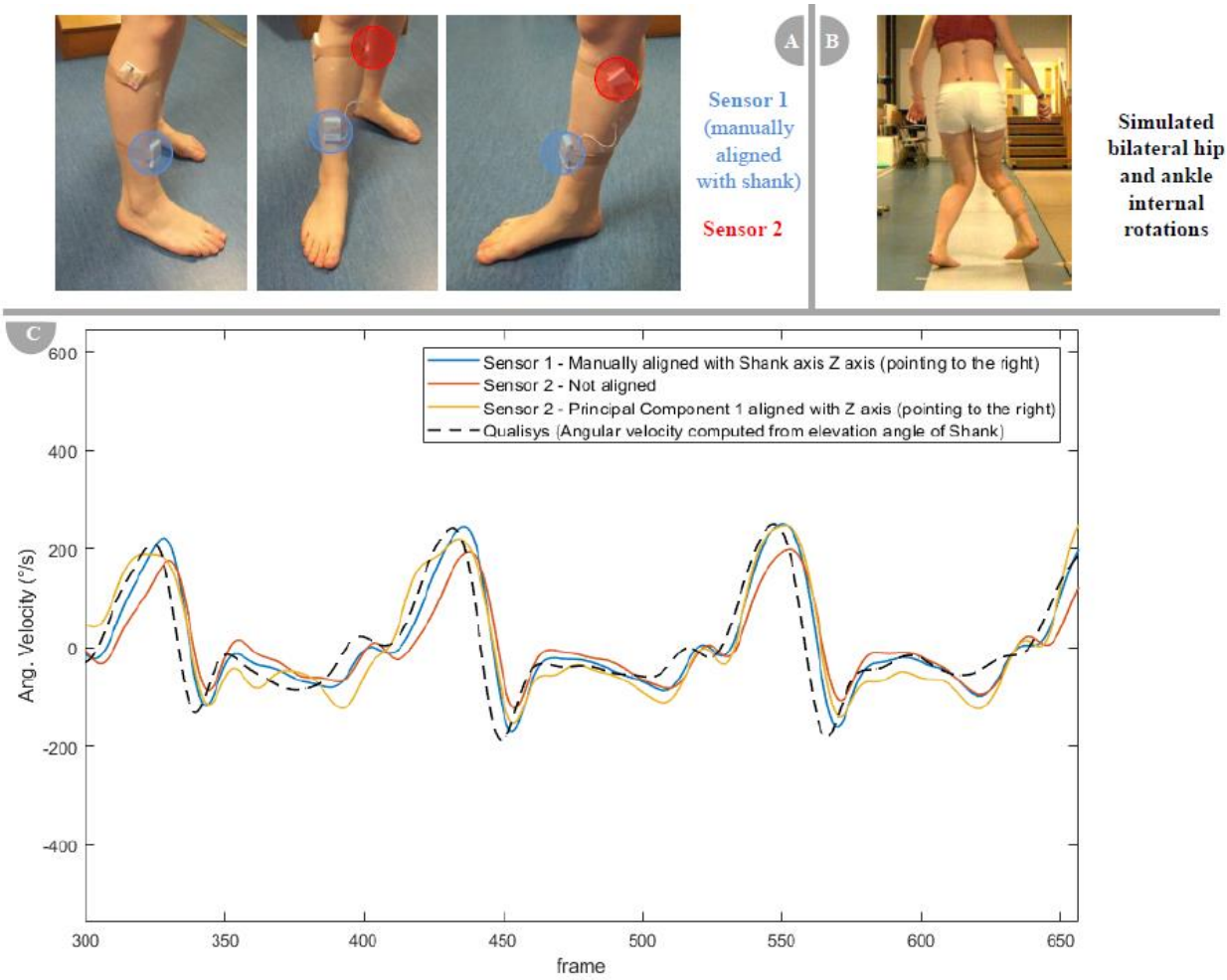
9.3.2 Regarding the wearable system

9.3.2.1 Leg length measurement

The double pendulum model proposed by Aminian et al. (2002) relies on leg length dimensions (thigh and shank segments lengths) measurements and assumes that the right and left legs have the same length. However, children with CP commonly present leg length discrepancy due to angular and torsional bone deformities or joint contractures (Riad et al., 2010; Sabharwal and Kumar, 2008). The main difference in leg length between the affected and non-affected side of a hemiplegic child occurs at the shank level (Riad et al., 2010). Furthermore, leg length measurement can be challenging with bone deformities and joint contractures (Sabharwal and Kumar, 2008). These combined, one can understand that potential bias is introduced due to the model for stride length estimation. As an illustration of the error induced by erroneous leg length measurement, stride length of a healthy control subject have been computed with two different shank lengths: the measured shank length and a simulated false shank length 1cm away from the measured one (representing 1.3% of the subject's leg length). The induced error was 2cm (1.7% of the original stride length) for stride length estimation.

9.3.2.2 Sensor to body segment alignment

A calibration method based on PCA was adopted as an optimal solution since a classic approach based on functional calibration (Favre et al., 2009) using a pre-defined set of movements was difficult to be envisaged for children with functional disabilities, especially in a home environment without the supervision of the investigator. PCA alignment method is based on the assumption that the pitch angular velocity is maximal in the sagittal plane during forward walking. This assumption may have induced potential errors especially for the children with a high level of impairment, with higher frontal and transverse components at shank and thigh levels during walking. These errors may have biased shank and thigh angles computation; hence the walking speed and other gait characteristics parameters estimation for which the angular velocity rate was used to be computed. Nevertheless, a quick experiment has proven that the angular velocity signal shape was well restored after PCA alignment as compared to a sensor manually aligned on the segment's longitudinal axis and the angular velocity computed from the shank orientation with the optoelectronic system (Figure 55).



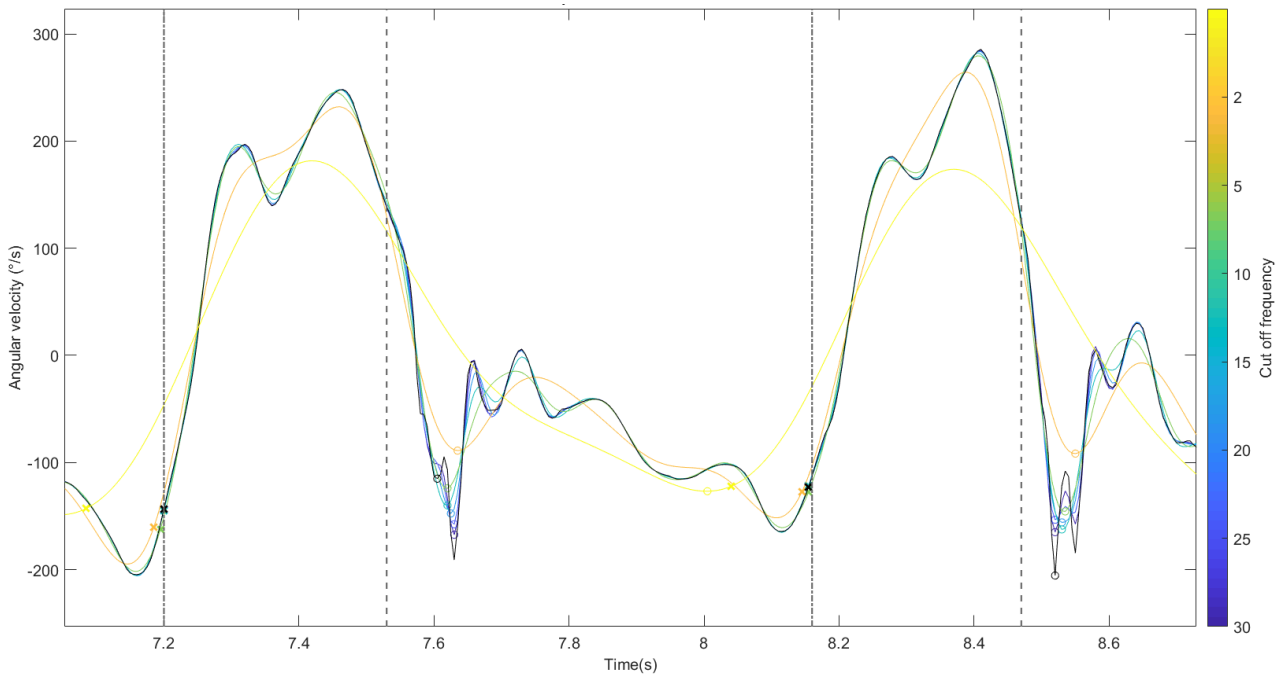
Signals are low-pass filtered (4th order Butterworth, cut off frequency 6 Hz).
The amplitude of the signal after PCA alignment (yellow) is more similar to the amplitude of the manually aligned sensor (blue) and the estimated angular velocity from the optoelectronic system (black) than the sensor that was not aligned (red).

Figure 55 –PCA alignment experiment. A) Sensor positioning; B) Protocol: walking with internal rotations; C) Angular velocity signals according to the sensor position and the alignment (manual or PCA)

9.3.2.3 Signal smoothness

Movement smoothness is variable according to the typology of CP (spastic, ataxic or dyskinetic). Abnormal rough patterns are commonly found in the distal part of the limbs (Berker and Yalçin, 2008). Variable signal smoothness can thus be found across the individuals with CP and the body segments. This heterogeneity was challenging to deal with.

The difficulty to detect events on inertial sensors data is directly linked to, first, the pattern of the signal and, second, its smoothness. In abnormal gait patterns, expected features of the signal (like peaks, zero-crossings, etc.) can be missing, and non-expected features (such as extra-peaks) can appear which decrease the algorithm performance for event detection. A compromise was to be found between reducing noise and keeping signal features of interest. Actually, for foot strike and foot off detection, we have noticed that the accuracy of gait events detection, with regard to the clinical reference (optoelectronic system and force plates), decreased according to the filter power applied (Figure 56). This is the reason why we did not apply supplementary filtering as compared to the filtering applied in the original methods (Mariani et al., 2010; Salarian et al., 2013, 2004). However, we consider that this could have been deeper investigated and probably personalized filtering could have been applied.



o*: foot strike;* x*: foot off. Back line represents the raw signal. Vertical lines represent reference gait events obtained with the clinical standard (optoelectronic system and force plates).*

Figure 56 - Effect of signal low pass filter (with Butterworth 4th order) on gait events detection according to the cut off frequency, on angular velocity during gait of a child with CP-GMFCS III

9.3.3 Regarding the protocol

Daily life monitoring in children is innovative. No consensual practices are currently available in the literature. We chose to monitor the participants for 3 days. Although a previous study proved that a minimum of 6 days was required to record stable measures of habitual ambulatory activity for the higher functioning children, and 4 days for the most affected children (Ishikawa et al., 2013), we thought that 3 days was constraining enough for the children, given the cumbersome sensor configuration (5 sensors) they had to wear. Indeed, a compromise was to be found to decrease the risk of patients' refusing to wear the sensors in their daily environment. One child was excluded from the study after being evaluated in laboratory settings due to the unwillingness to proceed with daily life measurements.

In addition, one weekend day was included in these 3 days of measurement. It is well known that physical activity during weekend differs from the rest of the week (Gerber et al., 2019; Rowlands et al., 2008; van Wely et al., 2012) which is why we chose to include a weekend day for a fair representation of the daily life habit of the children. This choice is debatable. It may have influenced our results. First, as discussed in Chapter 5, unexpected cyclical activities like biking, playing on swings or cross country skiing have the potential to induce false walking bout detection. These activities are more likely achieved during the weekend. Second, some of the children may have less time constraint during the weekend than the week, and thus may walk slower during weekend. This could have shifted the overall walking speed distribution toward lower values.

Moreover, the protocol for daily life measurements was set up late. The first participants were indeed recorded in the laboratory before having finalized the choice for sensor configuration, sensor fixation and the final protocol for daily life monitoring. Furthermore, parts of the participants were also involved in subsequent reliability (Gerber et al., 2019) and interventional studies, which timeline protocol was constrained by school holidays and logistic issues (number of available sensors). Thus the delay between the two assessments (laboratory and daily life) was of 7±3 months in average. Actually, one of the children with CP underwent surgery in the meantime which forced us to exclude him from the study to ensure that none of the children

substantially changed between both measurements. Moreover, during childhood, bone can grow until 1cm per year (Westh and Menelaus, 1981), so we had to take leg length dimensions twice, doubling the potential error related to leg length measurement described above (9.3.2.1).

9.4 Perspectives

The results of this thesis together with current research and development open new perspectives for the evaluation of pathological gait in ecological conditions. Many potential areas of technical and clinical investigations are available. Some general trails for future work are proposed in the following paragraphs.

9.4.1 Technical perspectives

9.4.1.1 Toward personalization of algorithms

As discussed in Chapter 5, the personalization of computational methods is highly relevant to refine biomechanical assumptions required for gait analysis. A relevant perspective of the work proposed in this thesis would be to explore the signal, or combined signals (e.g. the shank and the thigh), patterns recorded in clinical settings for features recognition in the signals recorded in natural settings. Walking bout detection, strides detection, gait events identification and also sensor alignment could be improved by matching the signals. Nevertheless, since gait in the laboratory is not the reflection of gait in daily life, a similar protocol as proposed in Chapter 5, including various speeds and also dual tasks in the laboratory, is recommended to cover the variations in daily life. Furthermore, an estimate of the real-world speed using a GNSS can be used to help the customized algorithm to adapt to the real-world speed.

9.4.1.2 Towards better accuracy in CP

Individuals with CP can present a wide range of anatomical and functional abnormalities. The priority perspective for gait analysis in children with CP using wearable sensors is to set up new protocols tailored to biomechanical constraints proper to CP. For example, further work could draw its inspiration from the work of Cutti et al. regarding sensor alignment (Cutti et al., 2010). They proposed to define IMU's orientation while the subject is in a predefined posture that can be supine with hip and knee flexion to suit for subjects with joint contractures (Figure 57).

Figure 57 - Calibration posture adapted to individuals with joint contractures proposed by Cutti et al. (2010)

To go further, several simple postures like this could be proposed for functional calibration. This would allow increasing the accuracy of gait parameters and would also give the possibility to compute more parameters highly relevant in CP, like 3D joint kinematics.

Moreover, recent studies have demonstrated the high potential of machine learning techniques in the field of gait analysis in children with CP for diverse purposes: activity recognition (Ahmadi et al., 2018; Hegde et al., 2018), GMFCS level identification (Schwartz and Munger, 2018) and gait event detection (Kidzińskiid et al., 2019; Lempereur et al., 2019). These approaches generally outperformed previous, commonly used, methods. Hence, applying these powerful statistical methods on IMU data could be helpful to reach high level of accuracy for gait analysis of children with CP.

9.4.1.3 Towards reduced sensor configuration

Single sensor configurations like trunk, waist or wrist-mounted sensors (Anisoara Paraschiv-Ionescu et al., 2019; Soltani et al., 2019; Zijlstra and Hof, 2003), have been developed but were not chosen in this work since fewer gait parameters were computable with these for children with CP. Minimizing the number of sensors is however needed to increase acceptability and compliance. Future work in this direction is indeed required to enable increasing the number of monitoring days. One idea should be to estimate a non-sensed body segment position or orientation from a sensor placed on another body segment. Lower limb (ankle, knee and hip) kinematics can indeed be considered as a chain where one joint is coupled with the others (Dejnabadi et al., 2008). For example, excessive knee flexion is necessarily associated with hip and ankle flexion to ensure sufficient stability in standing up. Biomechanical, statistical and machine learning approaches should be appropriate to do so (Dejnabadi et al., 2008; Kutilek and Viteckova, 2012).

9.4.1.4 Towards new sensors

We have addressed in a previous section the absence of knowledge of the walking context (e.g. outdoor/indoor, location, curved path, surface, etc.) which constitutes a major drawback in daily-life monitoring. The addition of new sensors could thus help getting more information about the contexts. For instance, a GNSS receiver can give appropriate estimation of the location and information about the environment can thus be deduced (indoor, outdoor, park, street, home, school, etc.). This idea was exploited by various authors and notably Wang and Adamczyk (2019), who used GNSS data to identify frequently repeated paths in order to include only frequently repeated walking bouts. Barometric pressure, embedded in insoles could also be advised to estimate load carriage (e.g. schoolbag). A microphone can identify if the subject walks in a crowded or empty environment (Wang and Adamczyk, 2019). Weather records could also be relevant to integrate weather conditions to the analysis. Besides, other sensors could be relevant to add, to record more gait parameters such as muscle and cardiac activities with EMG and electrocardiography sensors. Keeping in mind the need of a reduced sensor configuration, smart textiles integrating multimodal sensors constitute a potential relevant solution (Mečņika et al., 2014).

9.4.2 Clinical perspectives

9.4.2.1 Integrating performance assessment into the clinical process

First, the clinical perspective resulting from this work is the integration of dual task protocols during CGA. This has proven to be a simple way to reflect challenging situations, and underestimated difficulties may become apparent during dual tasks. Second, the main clinical perspective of this work is to evaluate the feasibility of using an ambulatory system in a clinical process. This perspective was actually applied in rehabilitation during the clinical trial of the Leenaards project (project to which this thesis was integrated to, cf. Preamble of the thesis) at CHUV in which I took part. We aimed at knowing how well physiotherapists can be guided by daily-life outputs in setting up a performance-based rehabilitation program, and can the effect of a rehabilitation program be reflected by ambulatory analysis outputs. A pilot interventional study was carried out for this purpose. A multiple single-case A-B-A study design was set as follows.

A. Baseline: each participant underwent an initial 10-consecutive-hour assessment of performance metrics with the wearable system from what were extracted performance metrics related to the gait function and physical activity. A standardized physical examination (GMFM 66) was also performed by a trained research physiotherapist. Based on the extracted metrics, a home-based individualized training program aiming at increasing daily performance was devised by the physiotherapist. Specific aims of the program were thus oriented on daily-life tasks.

B. Intervention: after the run-in period a second assessment with the wearable system took place 4 weeks later. At this stage, the training program was instructed to the participant. The participant received an individualized list of objectives and exercises. The training was implemented for 4 weeks with a weekly video- or phone-call appointment with the physiotherapist to discuss progress and difficulties.
A. Reversal: at the end of the intervention, a third assessment took place, followed by a 4-week wash-out and a final assessment.
Fourteen children with CP have been included in this study. Positive feedbacks have been collected from the physiotherapists, the families, and the children. However, several drawbacks surfaced so conclusions regarding the integration of daily-life data into the clinical process were difficult to set. The major drawbacks were the following.

- The robustness of sensors was insufficient for such a protocol. Problems occurred on several occasions with the sensors (e.g. not turning on) that consequently had to be repaired (reboot of the sensor's software) or replaced, which disrupted the strict time trial schedule of some of the patients.
- The extracted metrics from baseline measurement were not patient-specific, they did not vary according to the child's level of impairment or the child's needs.
- Physiotherapists did not always follow the instructions for devising the training objectives. Some of the objectives were not specific, measurable, achievable, relevant, or time-bound (SMART criteria) and some others were not daily-life oriented.
- Families' motivation varied a lot. Children who lived in an environment where the parents and the caregivers pushed them to complete their objectives had better results than the others.

Overall, according to these issues, it was difficult to prove the effect of ambulatory analysis outputs in rehabilitation at the group level. However, several observations were done at individual levels. For instance, three participants with GMFCS level III increased significantly their percentage of time walking per day, beyond the minimal detectable change previously documented (Gerber et al., 2019), after the individualized treatment (comparison between pre and post-intervention phases). Analyses are still ongoing but may result in weak conclusions given the heterogeneity of the children, of the physiotherapists' understanding and method during the study. The above-listed drawbacks constitute the main axes of improvement for a future clinical trial of this type. For instance:

- More robust sensors should be used (e.g. new generation of Physilogs (GaitUp, Renens, Switzerland)),
- The investigator should set the goals with the physiotherapist to ensure that they are SMART and performance-oriented,
- The extracted metrics should be in accordance with the training program's goals,
- The investigator should be informed about the daily environment and family situation, through questionnaires and/or interviews,
- A control group (children with CP without intensive training) should also be considered

9.4.2.2 Application to other clinical purposes in CP

Gait was the central focus of the doctoral work but, as mentioned in the introduction chapter, one-third of the children with CP cannot walk. Information about the habitual physical activity of these children may also be of high clinicians' interest, in order to highlight the relation between movement and well-being. Consensus exists on the link between physical activity and quality of life but is mainly based on indirect measures of physical activity only and focused on ambulatory children with CP (Mann et al., 2016; Omura et al., 2018). Further work examining the link between physical activity, continuously measured by wearable sensors, and objective and subjective data on quality of life and participation of children with CP with highly limited motor functions (GMFCS IV and V) could then constitute a concrete perspective of the current work. This study could take the form of an observational cross-sectional study with the following specific objectives: to quantify

the time spent in sedentary and in motor behaviors (passive or active), to quantify the intensity of motion and activity, and to quantify the diversity of postures (lying, sitting, standing) during children's daily life. A barcode of activity intensity such as the one proposed by Paraschiv-Ionescu et al. (2012) could be relevant for this application. The secondary objective would be to link these quantities to subjective data on well-being and global health (questionnaires). A reduced sensor configuration should be used as compared to the configuration proposed in the thesis. This project was actually submitted to the Science for Smiles foundation (Villeneuve, Switzerland) but has not been supported yet.

9.4.2.3 Application to other populations

Performance (daily-life) assessment as realized during this thesis can be relevant for many other pathologies. As a precise example, patients recovering from a total knee arthroplasty would beneficiate as much as patients with CP from the chosen sensor configuration, given the possibility to directly compute the knee range of motion. Indeed, as compared to healthy people, patients who underwent a total knee arthroplasty show functional deficits such as reduced walking speed, stride length and knee range of motion, inducing compensatory patterns in involved joints (Komnik et al., 2015). Ambulatory monitoring of their recovery may thus be highly helpful for the clinicians in order to nail the eventual persistence of functional deficits and prevent their definitive establishment. This project is actually supported by the HUG research foundation ('Projets de recherche et developpement') and is running since October 2019.

Clearly, a lot of other pathologies could beneficiate from objective performance assessment. In recent publications, elderly people, patients with neurological pathologies, such as PD, Multiple Sclerosis, and Stroke, have begun to be monitored in daily life for clinical research purposes (Brodie et al., 2015; Del Din et al., 2016a; S K Prajapati et al., 2011; Supratak et al., 2018; Takayanagi et al., 2019; Toosizadeh et al., 2015; Tudor-Locke et al., 2013; Warmerdam et al., 2020).

9.5 Final conclusion

This doctoral work aimed to study the gap between gait capacity and gait performance in the population of children with CP. We have adopted a progressive approach consisting of, first, assessing children's gait in the laboratory under challenging situations, and, second, assessing the children's gait in their daily life. This project was ambitious given the little methodological evidence accessible at the beginning of the thesis regarding gait monitoring of children with CP outside of the laboratories. This is why two methodological studies were undertaken at the beginning. Several obstacles were faced in relation to the atypical and heterogeneous characteristics of children with CP, resulting in various choices and approximations which should be of interest for future researches. The relevance of the personalization of data processing was also underlined. On a clinical point of view, the objective comparison of gait characteristics in various contexts has brought new knowledge about the difficulties of children with CP. It appeared that the challenging situations induced by dual tasks greatly penalize the children with CP. In contrast to recent studies establishing the link between capacity and performance on the basis of different metrics, the results of this thesis demonstrated thigh links between both activity constructs when they are evaluated with similar metrics. But this represented one single stone among all those necessary to build the bridge between the laboratory and real life. Several other studies must be undertaken to confirm these and bring new findings.

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Thesis: "*Gait analysis of children with cerebral palsy: bridging the gap between the laboratory and real life*"

2009 - 2014 *Compiègne, France*
Biological engineering studies (Master of Science) at the French top school "Université de Technologie de Compiègne", specialization in biomechanics and biomaterials

Professional experience

2018 - 2019 *Lausanne, Switzerland*
Research assistant at the pediatric Neurology and Neurorehabilitation Unit under the supervision of Dr. Newmann C.J.
- Clinical trial project management: Feasibility to use inertial sensors in rehabilitation programs. Collaborations: GaitUp SA (Switzerland), EPFL, HUG
- Supervision of 2 master students

2015- 2019 *Geneva, Switzerland*
Research assistant at Willy Taillard laboratory of kinesiology under the supervision of Dr. Armand A.
- Lead of several clinical research projects on gait analysis (mostly with inertial sensors). Collaborations: GaitUp SA (Switzerland), EPFL, CHUV
- Supervision of 2 master students
- Clinical Gait Analysis (CGA) activity: data acquisition, treatment and interpretation

2014 –2015 *Coubert, France*
Engineer mission head of the Laboratory of Movement Analysis of Coubert rehabilitation center under the supervision of Dr. Kocer S.
- CGA activity: data acquisition, treatment and interpretation
- Team management, project management, protocol set up, data organization

Feb.-August 2014 *Geneva, Switzerland*
End-of-studies internship at Willy Taillard laboratory of kinesiology under the supervion of Dr. Armand S. and Prof. Marin F.

Feb.-August 2013 *Waterloo, Canada*
Internship at the **Center for Contact Lens Research**, University of Waterloo under the supervision of Prof. Gorbet M.

Miscellaneous

Research contributions 10 oral and poster presentations in national and European conferences; 3 publications as first author, 2 publications as co-author in peer-reviewed journals,
Papers reviewing,
Grants applications (1 accepted – 20'000 CHF)

Awards Jury's "coup de Coeur" award – Hackathon of the Geneva University Hospitals 2018
Awards of Best poster (PEM 2016, Nancy), Best student presentation (SOFAMEA 2019, Grenoble)

Trainings Good Clinical Practice, Gait analysis course (ESMAC 2016, Sevilla), Statistic methods, Scientific writing

Skills

Languages	**English**: Fluent (7 months in Waterloo, ON, Canada / TOEIC score: 865) **Spanish**: Professional (6 months of studies in "Universidad de Zaragoza")
Software	Matlab, Rstudio, SPSS, motion analysis softwares (Mokka, Qualisys Track Manager, Nexus, visual 3D)
Computer languages	Matlab, R and HTML programming

Personal interests

Sport & Hobbies	Lindy hop dancing (practicing & teaching), swimming, yoga, outdoor activities (hiking, cross-country skiing). Formerly: Gymnastics (competitions, referring and teaching)

Journal publications

Accepted

Carcreff L., Bonnefoy-Mazure A., De Coulon G., Armand S. Analyse quantifiée de la marche, Movement & Sport Sciences – Science & Motricité, 2016, vol. 3, num. 93, p.7-21.

Attias M., Bonnefoy-Mazure A., Tabard A., Carcreff L., Hoffmeyer P., De Coulon G., Armand S. Analyse quantifiée de la marche, Movement & Sport Sciences – Science & Motricité, 2016

Carcreff L., Gerber C., Paraschiv-Ionescu A., De Coulon G., Newman C.J., Armand S., Aminian K. What is the best configuration of wearable sensors to measure spatiotemporal gait parameters in children with cerebral palsy?, Sensors, 2018, vol. 18, num. 2

Carcreff L., Fluss J., Allali G., Valenza N., Aminian K., Newman C.J., Armand S. The effects of dual tasks on gait in children with cerebral palsy, Gait and Posture, 2019, vol. 70, p.148-155

Paraschiv-Ionescu A., Newman C.J., Carcreff L., Gerber C., Armand S., Aminian K. Locomotion and cadence detection using a single trunk-fixed accelerometer: validity for children with cerebral palsy in daily life- like conditions, Journal of NeuroEngineering and Rehabilitation, 2019, vol. 16, num. 1, p.16-24

Gerber C., Carcreff L., Paraschiv-Ionescu A., Armand S., Newman C.J. Reliability of single-day walking performance and physical activity measures using inertial sensors in children with cerebral palsy, Annals of Physical and Rehabilitation Medicine, 2019, p. 2-7

Carcreff L., Paraschiv-Ionescu A., Gerber C., Newman C.J., Armand S., Aminian K. A Personalized Approach to Improve Walking Detection in Real-Life Set-tings: Application to Children with Cerebral Palsy, Sensors, 2019, vol. 19, num. 5316

Carcreff L., Gerber C.N., Paraschiv-Ionescu A., De Coulon G., Newman C.J., Aminian K. and Armand S. « Comparison of gait characteristics between clinical and daily life settings in children with cerebral palsy », Scientific reports, 2020, vol. 10, num. 2091, p. 1–11

Under review

Carcreff L., Gerber C.N., Paraschiv-Ionescu A., De Coulon G., Aminian K., Newman C.J., and Armand S. « Walking speed of children with cerebral palsy: laboratory versus daily life », in Journal of NeuroEngineering and Rehabilitation, submitted in December 2019

Conferences

Carcreff L., Bonnefoy-Mazure A., Valenza N., Allali G., Fluss J., Armand S.; *Influence of cognitive-motor interference on gait spatiotemporal parameters in children and adolescents with cerebral palsy: A preliminary study.* Annual meeting of European Society of Movement Analysis in Children and adults (ESMAC), Sevilla, Spain, 2016.

Carcreff L., Valenza N., Allali G., Aminian K., Fluss J., Armand S.; *Influence des interférences cognitivo-motrices sur la posture assise des enfants et adolescents avec une paralysie cérébrale.* Meeting « Posture – Equilibre – Mouvement » congress of

the Société Francophone Posture Equilibre, Locomotion (SOFPEL), European Society for Clinical Evaluation of Balance Disorders (ESCEBD) and Société Francophone d'Analyse du Mouvement chez l'Enfant et l'Adulte (SOFAMEA), Nancy, France, 2016. (best poster award)

Carcreff L., Valenza N., Allali G., Aminian K., Fluss J., Armand S.; *Influence of cognitive-motor interference on sitting posture of children and adolescent with cerebral palsy.* Annual meeting of the European Academy of Childhood Disability (EACD), Amsterdam, The Netherlands, 2017.

Carcreff L., Paraschiv-Ionescu A., Gerber C., De Coulon G., Aminian K., Newman C.J., Armand S.; *Assessment of the spatio-temporal gait parameters of children with cerebral palsy in daily-life settings: comparison between wearable systems using different sensor location.* Annual meeting of European Society of Movement Analysis in Children and adults (ESMAC), Trondheim, Norway, 2017.

Carcreff L., Paraschiv-Ionescu A., Gerber C., De Coulon G., Aminian K., Newman C.J., Armand S.; *Assessment of the spatio-temporal gait parameters of children with cerebral palsy in daily-life settings: comparison between wearable systems using different sensor location.* BioEngineering day at EPFL, Lausanne, Switzerland, 2017.

Carcreff L., Paraschiv-Ionescu A., Gerber C., De Coulon G., Aminian K., Newman C.J., Armand S.; *Better understand locomotor difficulties encountered in daily-life by children with cerebral palsy: sensor configuration and measurement accuracy.* Annual meeting of the Swiss Academy of Childhood Disability (SACD), Aarau, Switzerland, 2017.

Carcreff L., Paraschiv-Ionescu A., Gerber C., De Coulon G., Aminian K., Newman C.J., Armand S.; *Assessment of the spatio-temporal gait parameters of children with cerebral palsy in daily-life settings: comparison between wearable systems using different sensor location*. Annual research day of the Département Femme-mère-enfant of the Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland, 2018.

Carcreff L., Valenza N., Allali G., Aminian K., Newman C.J., Fluss J., Armand S.; *Influence des tâches cognitives sur la marche des enfants et adolescents avec une paralysie cérébrale*. Annual meeting of the Société Francophone d'Analyse du Mouvement chez l'Enfant et l'Adulte (SOFAMEA), Toulouse, France, 2018.

Carcreff L., Gerber C., Ionescu A., Aminian K., Newman C., Armand S. ; *Comparaison entre la capacité et la performance de marche chez les enfants atteints de paralysie cérébrale, basée sur la vitesse de marche.* Annual meeting of the Société Francophone d'Analyse du Mouvement chez l'Enfant et l'Adulte (SOFAMEA), Grenoble, France, 2019. (best student presentation award)

Carcreff L., Gerber C., Ionescu A., Aminian K., Newman C., Armand S. ; *La vitesse de marche des enfants atteints de paralysie cérébrale : vie quotidienne versus laboratoire*. Annual research day of the Département Femme-mère-enfant of the Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland, 2019.

Carcreff L., Ionescu A., Gerber C., De Coulon G., Aminian K., Newman C., Armand S. *Walking speed in children with cerebral palsy: Laboratory versus daily-life*. Annual meeting of the European Academy of Childhood Disability (EACD), Paris, France, 2019.