Bioinspired robotic rehabilitation tool for lower limb motor learning after stroke

by

Guillermo Asín Prieto

in partial fulfillment of the requirements for the degree of Doctor in Electrical, Electronics and Automation Engineering

Universidad Carlos III de Madrid

Advisors:

Juan Camilo Moreno Sastoque

José Luis Pons Rovira

Tutor:

María Dolores Blanco Rojas

November, 2019

To my big family.

ACKNOWLEDGEMENTS

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It is worth mentioning that the close and helpful collaboration with the *Centro de Referencia Estatal de Atención Al Daño Cerebral* (CEADAC) in Madrid (Spain); with the *Hospital Nacional de Parapléjicos de Toledo* (Spain); with the Intelligent Behavior Control Unit, in RIKEN Brain Science Institute in Nagoya (Japan); and with the Faculty of Medicine and the Faculty of Applied Science and Engineering, in the University of Toronto (Canada), constituted an essential asset for the successful progress of the work and studies presented in this thesis.

I want to show my gratitude to my advisors José Luis Pons and Juan Camilo Moreno, for their support and their great ideas. Sometimes, they have forced me to take important decisions that have given birth to this work and dissertation, and for that, although it has been quite hard, I thank them too.

I am grateful too to my tutor María Dolores Blanco for her patience with my e-mails, full of doubts more related to paperwork than to research; and to the *Universidad Carlos III de Madrid*, for giving me the opportunity to fulfill another step in my career

My gratitude goes too to Shingo Shimoda and Massimo Sartori, who has provided me with their reports required for the *Doctorado Internacional* distinction.

I want to thank all the colleagues and friends that have accompanied me in this journey, both in my group and from other groups, countries, institutions... Special mentions go to José González-Vargas for his great ideas, valuable support and prominent expertise that has greatly helped me in achieving this milestone in my career; to Filipe Oliveira

Barroso and Aitor Martínez-Expósito, thanks to them I have managed to perform the experiments, analyze the data, and extract conclusions, to finish the writing of this dissertation; and last but not least, to Eloy Urendes, whose help, ideas, and patience has been of inspiring help.

I am greatly grateful to all the volunteers that have made this work possible, both in development phase, suffering the pauses, the errors, and also enjoying the joy of seeing things work; and in the experimental phase, because without them, all the development would have been worthless.

I am extremely grateful to my family, because their support is greatly invaluable: to my parents, who have raised me with love and with a great sense of responsibility; to my sister, always lending me great moments and conversations and beers; to my brother, great friend, and also, and I am really proud of him, although being a bit younger than me, an example in my career. Indeed, I managed to achieve a personal milestone with his help: write a contribution with him as my co-author.

Special thanks to my soon-to-be-wife, Noelia, for her unconditional love, great support on the graphic art in this dissertation, understanding and huge patience, in these last steps of this work. You make this and all have sense.

Thanks also to those who helped me in this journey in any manner and I am forgetting to mention.

And last, but definitely not least, thank you God for everything.

Published, presented, and/or in preparation, contributions

The material from these sources included in this thesis is not singled out with typographic means and references. In order of appearance (prefix PC stands for Presented Contribution, all these contributions are partially included to different extends in this dissertation):

PC1. Robotic Platform with Visual Paradigm to Induce Motor Learning in Healthy Subjects [Asín-Prieto et al., 2017c].
Conference paper in "Iberian Robotics conference" (22-24, November, 2017, Sevilla, Spain) - ROBOT2017. Springer, Cham. This item is wholly included and adapted in this thesis.
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-70836-2_47`
Guillermo Asín-Prieto, Jose Gonzalez-Vargas, José Luis Pons and Juan Camilo Moreno.
I co-designed the experimental procedure, integrated the robotic platform, developed the controller and video game, performed these experiments, wrote the contribution and presented the results in the conference.
In chapter Introduction, from page 1; in chapter 1, section 1.3, from page 22; and in chapter 4, section 4.2, from page 87.

PC2. Pilot study: submaximal force control training for robotic therapy [Asín-Prieto et al., 2018b].
Conference paper in "School Advanced Neurorehabilitation" (September 16-21, 2018, Baiona, Pontevedra, Spain) - SSNR18. This item is partly included in this thesis.
Guillermo Asín-Prieto, Aitor Martínez-Expósito, José Luis Pons and Juan Camilo Moreno.
I designed the experimental procedure, integrated the robotic platform, developed the controller and video game, performed these experiments, wrote the contribution and presented the results in the conference.
In chapter Introduction, from page 1; in chapter 1, section 1.3, from page 22; and in chapter 4, section 4.4, from page 93.

PC3. Robot-mediated therapy to retrain ankle foot movements.
Book chapter in "Advances in Technology Assisted Neurorehabilitation". (To be published). Elsevier. This item is partly included in this thesis.
Guillermo Asín-Prieto, Aitor Martínez-Expósito, José Luis Pons and Juan Camilo Moreno.
I collaborated in the writing of the book chapter, providing the robotic and rehabilitation video games perspective, performed these experiments, and wrote about

the results.
In chapter Introduction, from page 1; and chapter 1, section 1.3.4, from page 32.

PC4. Emerging perspectives in stroke rehabilitation [Asín-Prieto et al., 2014a].
Book chapter in "Emerging Therapies in Neurorehabilitation" (2014). Springer, Berlin, Heidelberg. This item is partly included in this thesis.
The final authenticated publication is available online at https://doi.org/10.1007/978-3-642-38556-8.
Guillermo Asín-Prieto, Roberto Cano-de-la-Cuerda, Eduardo López-Larraz, Julien Metrot, Marco Molinari and Liesjet Elisabeth Henriette van Dokkum.
I collaborated in the writing of the book chapter, providing a robotic vision of the rehabilitation therapies focused on stroke.
In chapter 1, section 1.2.7, from page 17; and section 1.3, from page 22.

PC5. Modulation of muscle activity in tibialis anterior and gastrocnemius medialis applying novel force paradigms with a motorized ankle foot orthosis in healthy subjects
Journal paper under preparation. Provisional title. This item is wholly included and adapted in this thesis.
Guillermo Asín-Prieto, Filipe Oliveira Barroso, Aitor Martínez-Expósito, Eloy José Urendes, Jose Gonzalez-Vargas, Carlos González-Alted, José Luis Pons and Juan Camilo Moreno.
I designed the experimental procedure, integrated the robotic platform, developed the controller and video game, collaborated in the experiments, and collaborated in the writing of the contribution.
In chapter 1, section 1.3.4, from page 32; chapter 3, from page 71; and chapter 4, section 4.1, from page 84.

PC6. Joint stiffness tuning of exoskeleton robot H2 by tacit learning [Shimoda et al., 2015].
Conference paper in "International Workshop on Symbiotic Interaction" (October 7-8, 2015, Berlin, Germany) - Symbiotic15. Springer, Cham. This item is wholly included and adapted in this thesis.
The final authenticated publication is available online at https://doi.org/10.1007/978-3-319-24917-9_15
Shingo Shimoda, Álvaro Costa, **Guillermo Asín-Prieto**, Shotaro Okajima, Eduardo Iáñez, Yasuhisa Hasegawa and Juan Camilo Moreno.
I collaborated in the integration of the tacit adaptability algorithm with the current exoskeleton controller, and provided information on the current exoskeleton for the writing of the paper.
In chapter 2, section 2.1, from page 45.

PC7. BioMot Project: PROJECT FINAL REPORT (2016) [BioMot Consortium, 2016].
Project deliverable. This item is partly included in this thesis.

BioMot Consortium.
As part of the BioMot Consortium, I wrote the parts related to the exoskeleton, partly about the controller, and about the integration of several sensors on the exoskeletons.
In chapter 2, section 2.1, from page 45.

PC8. BioMot exoskeleton-Towards a smart wearable robot for symbiotic human-robot interaction [Bacek et al., 2017b].
Conference paper in "International Conference on Rehabilitation Robotics" (July 17-20, 2017, London, UK)- ICORR17. IEEE. Copyright ©2017, IEEE. This item is partly included in this thesis.
The final authenticated publication is available online at `https://doi.org/10.1109/ICORR.2017.8009487`
Tomislav Baček, Marta Moltedo, Kevin Langlois, **Guillermo Asín-Prieto**, María del Carmen Sánchez-Villamañán, Jose Gonzalez-Vargas and Juan Camilo Moreno.
I codeveloped the basic control of the exoskeleton and collaborated in the writing of the related sections of the contribution.
In chapter 2, section 2.2, from page 51.

PC9. BioMot Project: Deliverable D6.3 - BioMot optimized and integrated prototypes (2016) [Asín-Prieto et al., 2016a].
Project deliverable. This item is partly included in this thesis.
Guillermo Asín-Prieto, Jose Gonzalez-Vargas and Juan Camilo Moreno.
I collaborated in the writing of the exoskeleton and controllers related sections of this deliverable.
In chapter 2, section 2.2, from page 51.

PC10. Tacit Adaptability of a Mechanically Adjustable Compliance and Controllable Equilibrium Position Actuator, a Preliminary Study [Asín-Prieto et al., 2017d].
Conference paper in "International Symposium in Wearable Robots" (October 18-21, 2016, La Granja, Segovia, Spain) - WeRob2016 - Wearable Robotics: Challenges and Trends (2017). Springer, Cham. This item is partly included in this thesis.
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-46532-6_44`
Guillermo Asín-Prieto, Shingo Shimoda, Jose Gonzalez-Vargas, María del Carmen Sánchez-Villamañán, José Luis Pons and Juan Camilo Moreno.
I codeveloped the control of the actuator, performed these experiments, and wrote the contribution.
In chapter 2, section 2.2, from page 51; and section 2.3, from page 58.

PC11. Experimental analysis of tacit adaptability for control of compliant actuators [Asín-Prieto, 2016a].
Poster in "School and Symposium Advanced Neurorehabilitation" (June 6-10,

2016, Baiona, Pontevedra, Spain) - SSNR16
Guillermo Asín-Prieto. This item is partly included in this thesis.
I codeveloped the control of the actuator, performed these experiments, and elaborated the poster.
In chapter 2, section 2.3, from page 58.

PC12. Joint stiffness modulation of compliant actuators for lower limb exoskeletons [Gonzalez-Vargas et al., 2017].
Conference paper in "International Conference on Rehabilitation Robotics" (17-20 July, 2017, London, UK) - ICORR17. IEEE. Copyright ©2017, IEEE. This item is wholly included and adapted in this thesis.
The final authenticated publication is available online at `https://doi.org/10.1109/ICORR.2017.8009426`
Jose Gonzalez-Vargas, Shingo Shimoda, **Guillermo Asín-Prieto**, José Luis Pons and Juan Camilo Moreno.
I codeveloped the basic control of the exoskeleton and collaborated in the writing of the related sections of the contribution.
In chapter 2, sections 2.3 and 2.4, pages 58 and 65 respectively.

PC13. BioMot Project: Deliverable D7.3 - Report on experimental scenarios III (2016) [del Ama et al., 2016].
Project deliverable. This item is partly included in this thesis.
Antonio José del-Ama, Elisa Piñuela-Martín, Soraya Pérez-Nombela, Vicente Lozano-Berrio, Ángel Gil-Agudo, Eduardo Iáñez, **Guillermo Asín-Prieto**, Jose Gonzalez-Vargas and Juan Camilo Moreno.
As part of the BioMot Consortium, I wrote the parts related to the exoskeleton, partly about the controller, and about the integration of several sensors on the exoskeletons.
In chapter 2, section 2.4, from page 65.

PC14. Robotic Platform including a Visual Paradigm to Promote Motor Learning [Asín-Prieto et al., 2017b].
Conference paper in "School and Symposium Advanced Neurorehabilitation" (September 17-22, 2017, Baiona, Pontevedra, Spain) - SSNR17. This item is wholly included and adapted in this thesis.
Guillermo Asín-Prieto, Jose Gonzalez-Vargas, José Luis Pons and Juan Camilo Moreno.
I co-designed the experimental procedure, integrated the robotic platform, developed the controller and video game, performed these experiments, wrote the contribution and presented the results in the conference.
In chapter 4, section 4.2, from page 87.

PC15. *Plataforma Robótica con Paradigma Visual para Inducir Aprendizaje Motor en Sujetos Sanos* [Asín-Prieto et al., 2017a].

Conference paper in "IX *Congreso Iberoamericano de Tecnologías de Apoyo a la Discapacidad*" (November 22-24, 2017, Bogotá, Colombia) - Iberdiscap17. This item is wholly included and adapted in this thesis.
Guillermo Asín-Prieto, Jose Gonzalez-Vargas, José Luis Pons and Juan Camilo Moreno.
I co-designed the experimental procedure, integrated the robotic platform, developed the controller and video game, performed these experiments, and wrote the contribution.
In chapter 4, section 4.2, from page 87.

PC16. Haptic adaptive feedback to promote motor learning with a robotic ankle exoskeleton integrated with a video game
Journal paper sent to "Frontiers in Bioengineering and Biotechnology", under the Research Topic: "Somatosensory Integration in Human Movement: Perspectives for Neuromechanics, Modelling and Rehabilitation" (Under revision). This item is wholly included and adapted in this thesis.
Guillermo Asín-Prieto, Aitor Martínez-Expósito, Eloy José Urendes, Jose Gonzalez-Vargas, Filipe Oliveira Barroso, Fady Shibata Alnajjar, Carlos González-Alted, José Luis Pons and Juan Camilo Moreno.
I designed the experimental procedure, integrated the robotic platform, developed the controller and video game, collaborated in the experiments, and collaborated in the writing of the contribution.
In chapter 4, section 4.3, from page 91; and in chapter 5.

PC17. Feasibility of submaximal force control training for robot–mediated therapy after stroke [Asín-Prieto et al., 2018a].
Conference paper in "International Conference on Neurorehabilitation" (16-20, October, 2018, Pisa, Italy) - ICNR18. This item is partly included in this thesis.
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-030-01845-0_51`
Guillermo Asín-Prieto, Fady Shibata Alnajjar, Aitor Martínez-Expósito, Shingo Shimoda, José Luis Pons and Juan Camilo Moreno.
I designed the experimental procedure, integrated the robotic platform, developed the controller and video game, performed these experiments, wrote the contribution and presented the results in the conference.
In chapter 4, section 4.4, from page 93.

Other Research Merits

1. Monitoring stability of gait on exoskeletons based on proprioceptive information [Asín-Prieto et al., 2014c].
   Conference paper in "International Workshop in Wearable Robots" (September 4-19, 2014, Baiona, Pontevedra, Spain) - WeRob2014
   Guillermo Asín-Prieto, Eloy José Urendes, Juan Álvaro Gallego, Juan Camilo Moreno and José Luis Pons.
   I developed the adaptation of the algorithm to wearable exoskeletons, performed these experiments, analyzed the data and wrote the contribution.

2. Testing the generation of speed-dependent gait trajectories to control a 6DoF overground exoskeleton [Asín-Prieto et al., 2015b].
   Conference paper in "International Conference on Intelligent Robotics and Applications" (August 24-27, 2015, Portsmouth, UK) - ICIRA2015. Springer, Cham. The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-22876-1_42`.
   Guillermo Asín-Prieto, Shingo Shimoda, Jose Gonzalez-Vargas, José Luis Pons, Antonio José del-Ama, Ángel Gil-Agudo and Juan Camilo Moreno.
   I developed the adaptation of the algorithm to wearable exoskeletons, performed these experiments, analyzed the data and wrote the contribution.

3. Testing the generation of speed-dependent gait trajectories to control a 6DoF overground exoskeleton [Asín-Prieto, 2015].
   Poster in "School Advanced Neurorehabilitation" (September 13-18, 2015, Valencia, Spain) - SSNR15
   Guillermo Asín-Prieto.
   I developed the adaptation of the algorithm to wearable exoskeletons, performed these experiments, analyzed the data and prepared and presented the poster.

4. *Ensayos con trayectorias generadas dependientes de la velocidad de la marcha para controlar exoesqueletos con 6 grados de libertad*[Asín-Prieto et al., 2015a].
   Conference paper in "VIII *Congreso Iberoaéricano de Tecnologías de Apoyo a la Discapacidad*" (November 9-12, 2015, Punta Arenas, Chile) - Iberdiscap15
   Guillermo Asín-Prieto, Shingo Shimoda, Jose Gonzalez-Vargas, José Luis Pons, Antonio José del-Ama, Ángel Gil-Agudo and Juan Camilo Moreno.
   I developed the adaptation of the algorithm to wearable exoskeletons, performed these experiments, analyzed the data and wrote the contribution.

5. Tacit adaptability on submaximal force control for ankle robotic training [Asín-Prieto et al., 2019].
   Conference paper in "Wearable Robotics Association Conference" (Mach 26-28, 2019, Scottsdale, AZ, USA) - WearRAcon19

Guillermo Asín-Prieto, Eduardo Asín-Prieto, Aitor Martínez-Expósito, José Luis Pons and Juan Camilo Moreno.
I designed the experimental procedure, integrated the robotic platform, developed the controller and video game, performed these experiments, and wrote the contribution.

6. Tacit adaptability: EEG-informed symbiotic approach applied to rehabilitation robot control [Asín-Prieto, 2016b].
Poster in "Xmas Meeting" (December 22, 2016, Cajal Institute, Madrid, Spain)
Guillermo Asín-Prieto.
I contributed in the development of the controller.

7. Rehabilitation technologies for spinal injury [Asín-Prieto et al., 2016b].
Book chapter in "Emerging Therapies in Neurorehabilitation II". (2016). Springer, Cham.
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-24901-8`.
Guillermo Asín-Prieto, Amaia Ilzarbe Andrés, Anusha Venkatakrishnan, Wasim Qamar Malik, Volker Dietz and William Zev Rymer.
I collaborated in the writing of the book chapter, providing a robotic vision of the rehabilitation therapies focused on spinal cord injury.

8. *Estructura mecánica y actuación* [Villa Parra et al., 2017].
Book chapter in "*Exoesqueletos Robóticos para Rehabilitación y Asistencia de Pacientes con Daño Neurológico Experiencias y Posibilidades en Iberoamérica*" (2017) ISBN/ISSN 978-84-15413-29-5
Ana Cecilia Villa Parra, Teodiano Freire Bastos, Francisco Resquín, Juan Camilo Moreno, Ernesto Rodríguez-Leal, Karen Acosta, Sergio Casco, Eduardo Rocon, Antonio José del-Ama and **Guillermo Asín-Prieto**.
I collaborated in the writing of the book chapter, writing about the control of wearable exoskeletons for rehabilitation.

9. Human neural electrophysiological basics and its applications.
Workshop in "Madrid Global BrainHack 2018" (May 3-5, 2018, Madrid, Spain)
Aitor Martínez-Expósito and **Guillermo Asín-Prieto**.
I collaborated in the organization of the whole Madrid Global BrainHack event, and presented the robotic perspective of Brain Computer Interfaces.

10. A closed-loop brain-computer interface triggering an active ankle-foot orthosis for inducing cortical neural plasticity [Xu et al., 2014].
Journal paper in "IEEE Transactions on Biomedical Engineering" (March, 26, 2014)
The final authenticated publication is available online at `https://doi.org/10.1109/TBME.2014.2313867`.

Ren Xu, Ning Jiang, Natalie Mrachacz-Kersting, Chuang Lin, **Guillermo Asín-Prieto**, Juan Camilo Moreno, José Luis Pons, Kim Denstrup and Dario Farina.
I provided technical and scientific support on the use of the ankle exoskeleton for these experiments, and provided technical information for the writing of the paper.

11. NOTARIAL RECORD 4022/2017 - "*Software de monitorización y control de una ortesis robótica de tobillo y pie para rehabilitación de lesiones del sistema nervioso central*"
Registered by the *Unidad de Protección de Resultados y Promoción de EBTs del CSIC* (2017)
I developed the software, and provided technical information and graphics for the preparation of the application.

12. Physiological Evaluation of Different Control Modes of Lower Limb Robotic Exoskeleton H2 in Patients with Incomplete Spinal Cord Injury [Pérez-Nombela et al., 2017].
Conference paper in "International Conference in Neurorehabilitation" (October 18-21, 2016, La Granja, Segovia, Spain) - ICNR2016 - Converging Clinical and Engineering Research on Neurorehabilitation II (2017). Springer, Cham.
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-46669-9_58`.
Soraya Pérez-Nombela, Antonio José del-Ama, **Guillermo Asín-Prieto**, Elisa Piñuela-Martín, Vicente Lozano-Berrio, Diego Serrano-Muñoz, Ángel Gil-Agudo, José Luis Pons and Juan Camilo Moreno.
I developed the different control modes used for these experiments.

13. Muscle Activity and Coordination During Robot-Assisted Walking with H2 Exoskeleton [del Ama et al., 2017].
Conference paper in "International Conference in Neurorehabilitation" (October 18-21, 2016, La Granja, Segovia, Spain) - ICNR2016 - Converging Clinical and Engineering Research on Neurorehabilitation II (2017). Springer, Cham.
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-46669-9_59`.
Antonio José del-Ama, **Guillermo Asín-Prieto**, Elisa Piñuela-Martín, Soraya Pérez-Nombela, Vicente Lozano-Berrio, Diego Serrano-Muñoz, Fernando Trincado-Alonso, Jose Gonzalez-Vargas, Ángel Gil-Agudo, José Luis Pons and Juan Camilo Moreno.
I developed the different control modes used for these experiments.

14. Detection of Subject's Intention to Trigger Transitions Between Sit, Stand and Walk with a Lower Limb Exoskeleton [Trincado-Alonso et al., 2017].
Conference paper in "International Symposium in Wearable Robots" (October 18-21, 2016, La Granja, Segovia, Spain) - WeRob2016 - Wearable Robotics: Challenges and Trends (2017). Springer, Cham.

The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-46532-6_41`.
Fernando Trincado-Alonso, Antonio José del-Ama, **Guillermo Asín-Prieto**, Elisa Piñuela-Martín, Soraya Pérez-Nombela, Ángel Gil-Agudo, José Luis Pons and Juan Camilo Moreno.
I developed the different control modes used for these experiments.

15. *INTEGRACION DE INTERFAZ CEREBRO-COMPUTADOR Y EXOESQUELETO DE MIEMBRO INFERIOR ORIENTADO A LA REHABILITACION* [Costa et al., 2015].
Conference paper in "XXXVI *Jornadas de Automática*" (September, 2-4, 2015, Bilbao, Vizcaya, Spain)
Álvaro Costa, **Guillermo Asín-Prieto**, Shingo Shimoda, Eduardo Iáñez, Juan Camilo Moreno, José Luis Pons and José María Azorín.
I developed the different control modes used for these experiments and provided technical information for the writing of the paper.

16. An integrated lower limb exoskeleton and body weight support system: design and implementation [Urendes et al., 2014].
Conference paper in "International Workshop in Wearable Robots" (September 4-19, 2014, Baiona, Pontevedra, Spain) - WeRob2014
Eloy José Urendes, **Guillermo Asín-Prieto**, María Gómez, Ramón Ceres and José Luis Pons.
I contributed in the development of the integrated platform, supporting the exoskeleton module.

17. A flexible architecture to enhance wearable robots: integration of EMG-informed models [Ceseracciu et al., 2015].
Conference paper in "IEEE/RSJ International Conference on Intelligent Robots and Systems" (September 28 - October 2, 2015, Hamburg, Germany) - IROS2015
The final authenticated publication is available online at `https://doi.org/10.1109/IROS.2015.7353997`.
Elena Ceseracciu, Alice Mantoan, Marco Matteo Bassa, Juan Camilo Moreno, José Luis Pons, **Guillermo Asín-Prieto**, Antonio José del-Ama, Ángel Gil-Agudo, Ester Márquez-Sánchez, Claudio Pizzolato, David G Lloyd and Monica Reggiani.
I contributed in the development of the integrated platform and provided technical information for the writing of the paper.

18. The new generation of compliant actuators for use in controllable bio-inspired wearable robots [Bacek et al., 2017a].
Conference paper in "International Symposium in Wearable Robots" (October 18-21, 2016, La Granja, Segovia, Spain) - WeRob2016 - Wearable Robotics: Challenges and Trends (2017). Springer, Cham.
The final authenticated publication is available online at `https://doi.org/10.`

1007/978-3-319-46532-6_42.
Tomislav Baček, Marta Moltedo, Jose Gonzalez-Vargas, **Guillermo Asín-Prieto**, María del Carmen Sánchez-Villamañán, Juan Camilo Moreno and Dirk Lefeber.
I contributed in the development of the controllers for the actuators and provided technical information for the writing of the paper.

19. Symbiotic wearable robotic exoskeletons: the concept of the BioMot project [Moreno et al., 2014].
Conference paper in "International Workshop on Symbiotic Interaction" (October 30-31, 2014, Helsinki, Finland) - Symbiotic14. Springer, Cham.
The final authenticated publication is available online at https://doi.org/10.1007/978-3-319-13500-7_6.
Juan Camilo Moreno, **Guillermo Asín-Prieto**, José Luis Pons, Heidi Cuypers, Bram Vanderborght, Dirk Lefeber, Elena Ceseracciu, Monica Reggiani, Freygardur Thorsteinsson, Antonio José del-Ama, Ángel Gil-Agudo, Shingo Shimoda, Eduardo Iáñez, José María Azorín and Javier Roa.
I contributed in the writing of the paper.

20. Experimental architecture for synchronized recordings of cerebral, muscular and biomechanical data during lower limb activities [Iáñez et al., 2015].
Conference paper in the "23th Mediterranean Conference on Control and Automation" (June, 16-19, 2015, Torremolinos, Spain) - MED 2015. IEEE.
The final authenticated publication is available online at https://doi.org/10.1109/MED.2015.7158742.
Eduardo Iáñez, Álvaro Costa, Elena Ceseracciu, Ester Márquez-Sánchez, Elisa Piñuela-Martín, **Guillermo Asín-Prieto**, Antonio José del-Ama, Ángel Gil-Agudo, Monica Reggiani, José Luis Pons, Juan Camilo Moreno and José María Azorín.
I contributed in the writing of the paper.

21. An EMG-informed Model to Evaluate Assistance of the BioMot Compliant Ankle Actuator [Ceseracciu et al., 2017].
Conference paper in "International Symposium in Wearable Robots" (October 18-21, 2016, La Granja, Segovia, Spain) - WeRob2016 - Wearable Robotics: Challenges and Trends (2017). Springer, Cham.
The final authenticated publication is available online at https://doi.org/10.1007/978-3-319-46532-6_43.
Elena Ceseracciu, Luca Tagliapietra, Juan Camilo Moreno, **Guillermo Asín-Prieto**, Antonio José del-Ama, Soraya Pérez-Nombela, Elisa Piñuela-Martín, Ángel Gil-Agudo and Monica Reggiani.
I contributed in the development of the controllers for the actuators and provided technical information for the writing of the paper.

22. Attention level measurement during exoskeleton rehabilitation through a BMI system [Costa et al., 2017].

Conference paper in "International Symposium in Wearable Robots" (October 18-21, 2016, La Granja, Segovia, Spain) - WeRob2016 - Wearable Robotics: Challenges and Trends (2017). Springer, Cham.
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-319-46532-6_40`.
Álvaro Costa, **Guillermo Asín-Prieto**, Jose Gonzalez-Vargas, Eduardo Iáñez, Juan Camilo Moreno, Antonio José del-Ama, Ángel Gil-Agudo and José María Azorín.
I contributed in the development of the controllers for the actuators and provided technical information for the writing of the paper.

23. Theoretical Approach for Designing the Rehabilitation Robot Controller [Okajima et al., 2018]
Journal paper in "Journal of Advanced Robotics" (July, 5, 2019).
The final authenticated publication is available online at `https://doi.org/10.1080/01691864.2019.1633402`.
Shotaro Okajima, Fady Shibata Alnajjar, Álvaro Costa, **Guillermo Asín-Prieto**, José Luis Pons, Juan Camilo Moreno, Yasuhisa Hasegawa and Shingo Shimoda.
I collaborated in the integration of the tacit adaptability algorithm with the current exoskeleton controller.

24. Bioinspired control and actuation systems for symbiotic control of human gait assisting exoskeletons.
Workshop in "School and Symposium Advanced Neurorehabilitation" (September 17-22, 2017, Baiona, Pontevedra, Spain) - SSNR17
Guillermo Asín-Prieto.
I presented the advances on my research related to the topic of symbiotic control for exoskeletons.

25. Voluntary control of wearable robotic exoskeletons by patients with paresis via neuromechanical modeling [Durandau et al., 2019].
Journal paper in "Journal of NeuroEngineering and Rehabilitation" (July, 17, 2019).
The final authenticated publication is available online at `https://doi.org/10.1186/s12984-019-0559-z`.
Guillaume Durandau, Dario Farina, **Guillermo Asín-Prieto**, Iris Dimbwadyo-Terrer, Sergio Lerma-Lara, José Luis Pons, Juan Camilo Moreno and Massimo Sartori.
I contributed in the integration of the current exoskeleton controller with the algorithms for EMG decoding, provided support during the experiments, and contributed in the writing with technical details.

26. PATENT NUMBER WO2018178427A1
Robotised system for assisted functional joint rehabilitation

Juan Camilo Moreno, María del Carmen Sánchez-Villamañán, **Guillermo Asín-Prieto**, José Luis Pons, Carlos Fernández Isoird and Juan Antonio Martín Prado.
I contributed in the development of the control for the orthosis, and provided technical information for the application.

27. PATENT NUMBER ES1182486Y
Set of mechanical transmission equipment rehabilitation
Juan Camilo Moreno, María del Carmen Sánchez-Villamañán, **Guillermo Asín-Prieto**, José Luis Pons, Carlos Fernández Isoird and Juan Antonio Martín Prado.
I contributed in the development of the control for the orthosis, and provided technical information for the application.

28. Bioinspired control and actuation systems for symbiotic control of human gait assisting exoskeletons
Presentation in "*Jornadas Cajal Junior* 2017" (June, 15, 2017, Madrid, Spain)
Guillermo Asín-Prieto.
I presented the research of my Ph.D.

29. Fatigue Compensating Muscle Excitability Enhancement by Transcranial Magnetic Stimulation: A Case Report [San Agustín et al., 2018]
Conference paper in "International Conference on Neurorehabilitation" (16-20, October, 2018, Pisa, Italy) - ICNR18
The final authenticated publication is available online at `https://doi.org/10.1007/978-3-030-01845-0_168`
Arantzazu San Agustín Pérez, **Guillermo Asín-Prieto** and José Luis Pons.
I contributed on the development of the platform, adapting the video game to the upper-limb.

30. *Monitorización de la estabilidad de la marcha con exoesqueletos basada en información propioceptiva* [Asín-Prieto et al., 2014b].
Conference paper in "*Congreso Regional en Instrumentación Avanzada*" (December 17-19, 2014, San Carlos, Costa Rica) - CRIA14.
Guillermo Asín-Prieto, Eloy José Urendes, Juan Álvaro Gallego, Juan Camilo Moreno and José Luis Pons.
I developed the adaptation of the algorithm to wearable exoskeletons, performed these experiments, analyzed the data and wrote the contribution.

31. BioMot Project: Deliverable D4.1 - Physically based simulations with partial demonstrators I. (2014) [Asín-Prieto and Moreno, 2014].
Project deliverable.
Guillermo Asín-Prieto and Juan Camilo Moreno.
I collaborated in the writing of the exoskeleton related sections of this deliverable.

Resumen técnico

ESTA tesis doctoral presenta, tras repasar la marcha humana, las principales patologías y condiciones que la afectan, y los distintos enfoques de rehabilitación con la correspondiente implicación neurofisiológica, el camino de investigación que desemboca en la herramienta robótica de rehabilitación y las terapias que se han desarrollado en el marco de los proyectos europeos BioMot: *Smart Wearable Robots with Bioinspired Sensory-Motor Skills* y HANK: *European advanced exoskeleton for rehabilitation of Acquired Brain Damage (ABD) and/or spinal cord injury's patients*, y probado bajo el paraguas del proyecto europeo ASTONISH: *Advancing Smart Optical Imaging and Sensing for Health* y el proyecto nacional ASSOCIATE: *A comprehensive and wearable robotics based approach to the rehabilitation and assistance to people with stroke and spinal cord injury.*

Inicialmente se presenta la marcha humana, caracterizándola en arreglo a sus fases de apoyo y balanceo, y a los parámetros espaciotemporales, cinéticos y cinemáticos, sin dejar de lado los parámetros fisiológicos; para pasar a mostrar un repaso por las principales patologías o condiciones que afectan la marcha humana: lesión medular, parálisis cerebral, lesión cerebral traumática, deficiencias neuromusculares, enfermedades osteoarticulares, envejecimiento, e ictus o accidente cerebrovascular. A continuación, se enmarca la herramienta robótica que se desarrolla en esta tesis, en la rehabilitación para el ictus, fundamentando su uso en esta extendida patología debido a que afecta a 13,7 millones de personas cada año, y a que hay unos 80 millones de supervivientes, afectando a todos los rangos de edad. Además, el 80 % de las personas afectadas por un accidente cerebrovascular ven asimismo comprometida su capacidad motora, motivando la necesidad de desarrollar herramientas enfocadas en la rehabilitación y recuperación, hasta donde sea posible, de la independencia perdida por motivo de la enfermedad, con la marcha como componente fundamental de esa independencia.

Después de dar un repaso por la marcha y las características de la patología, se da un repaso explicativo por las tres fases de la terapia para rehabilitación de la marcha: T1) entrenamiento preparatorio basado en movilización de las articulaciones del miembro inferior; T2) recuperación de la marcha; y T3) mejora de la marcha con el objetivo de recuperar la movilidad para las actividades de la vida diaria. Se presenta esta clasificación de las fases para enmarcar el trabajo de esta tesis en las fases T1 y T2.

Debido a que la recuperación motora se basa en el aprendizaje motor, se da una breve introducción al mismo exponiendo su relación con la neuroplasticidad, y estableciendo que, para potenciar todo tipo de aprendizaje, es capital establecer un reto, esto es, una dificultad asumible, y que no sólo hace que la tarea de entrenamiento sea menos monótona, sino que además potencia el proceso de retención del aprendizaje. El aprendizaje motor, como todo aprendizaje, para poder tener lugar, requiere que haya plasticidad neuronal. La plasticidad neuronal se puede describir por medio de estos cuatro factores: 1) evolución de la representación neuronal para movimientos que requieren habilidad, que estaban latentes antes de la lesión; y reclutamiento de áreas sanas y que se usaban antes de que la lesión ocurriera, cuando la dificultad de la tarea era mayor; 2) mayor excitabilidad de las neuronas y más eficacia de la conexión sináptica; 3) cambios morfológicos asociados a los fenómenos de potenciación y depresión a largo plazo (LTP y LTD de sus siglas en inglés, *long term potentiation* y *long term depression* respectivamente); y 4) adaptación de las redes corticales, subcorticales y espinales que aún funcionan al movimiento aprendido. Hay distintos métodos no invasivos que permiten evaluar los cambios neuroplásticos (reflejo de Hoffman, onda F, potenciales motores evocados, etc), y dado que en esta tesis se han usado los potenciales motores evocados (MEPs, de sus siglas en inglés, *motor evoked potentials*), se presenta la estimulación magnética transcraneal (TMS, de sus siglas en inglés, *transcranial magnetic stimulation*), como la técnica utilizada para evocar en la corteza motora asociada al músculo o a los músculos, cuya excitabilidad corticoespinal se desea evaluar, un potencial motor, recogido por medio de electromiografía superficial. La técnica de TMS permite observar cambios en la excitabilidad corticoespinal antes y después de un tratamiento que potencialmente induzca un aprendizaje motor, para poder evaluar si estos cambios están relacionados con el tratamiento, así como permitiendo observar si son duraderos en el tiempo.

En el capítulo de la revisión de la literatura se introducen también las diferencias entre los enfoques clásicos de rehabilitación, y los ayudados por las tecnologías robóticas, mostrando que no hay un claro ganador en tal batalla, pero manifestando la ventaja de la tecnología al permitir medir de manera objetiva y ayudar a caracterizar el proceso de recuperación. Una vez introducida la tecnología robótica como tecnología para la rehabilitación, se presentan los exoesqueletos como la tecnología robótica más adecuada implicada en los enfoques rehabilitadores para la marcha, y se da un repaso por los dispositivos existentes, con sus características y limitaciones, para mostrar la motivación de este trabajo. Las limitaciones que presentan los dispositivos actuales relevantes son que: utilizan patrones pre-grabados; no tienen sistemas de retroalimentación visual, o sus sistemas de retroalimentación son demasiados simples, no presentando el potencial de un video juego: entretenimiento y adherencia al tratamiento, permitiendo modificar la dificultad. Algunos, por otro lado, son tan complejos que demandan un esfuerzo cognitivo difícil para los pacientes, o incluso son complejos de configurar y comandar, llevando al abandono de la tecnología tanto por parte de pacientes como por parte de terapeutas. Además, la mayoría de ellos carecen de la capacidad de introducir aleatoriedad en el tratamiento, potencialmente desembocando en el aburrimiento del paciente, y en el abandono de la terapia en última instancia. Por último, pero no por ello menos importante, las tareas que proponen no se adaptan a lo largo del entrenamiento a las capacidades y recuperación del sujeto.

Por ello, la herramienta que se propone en esta tesis consta de la integración de un tobillo robótico fijado a una plataforma, con una retroalimentación visual por medio de un video juego diseñado para entrenar los movimientos en el plano sagital del tobillo: dorsiflexión y plantarflexión; con el sujeto sentado. La herramienta es capaz de generar patrones de par controlados que perturban las trayectorias seguidas por el sujeto, dificultando la tarea de recoger los ítems en pantalla. Además, la magnitud de estas perturbaciones depende del rendimiento durante la tarea, incrementando la dificultad cuando el rendimiento va mejorando, consiguiendo imponer un reto continuo, potenciando la adherencia al tratamiento así como su eficacia para fomentar la retención de lo aprendido.

Tras exponer la revisión de la literatura, se presenta el desarrollo de la herramienta de rehabilitación, recorriendo el camino desde la prueba de los algoritmos de control, hasta el desarrollo del video juego y diseño del protocolo experimental, pasando por la adecuación del control al actuador *compliant* en que se basa la herramienta, o las pruebas primero en banco de pruebas y después con sujetos sanos vistiendo el dispositivo.

El primer estudio que se presenta consiste en aplicar un algoritmo, bioinspirado, de aprendizaje autónomo, utilizado en bípedos (los cuales presentan la capacidad de aprender a caminar sin conocimiento previo de la tarea ni del entorno, únicamente conociendo algunos puntos de la trayectoria angular a realizar por las articulaciones), a un exoesqueleto con seis grados de libertad actuados, con actuadores rígidos, en el plano sagital, correspondiendo con las tres principales articulaciones del miembro inferior, esto es, cadera, rodilla y tobillo. Esta adaptación del algoritmo permite modular la rigidez de un actuador rígido con una implementación sencilla. Se acuñó el término adaptabilidad tácita (TAd, de sus siglas en inglés, *tacit adaptability*) para referirse a esta estrategia de control.

El segundo estudio que se presenta tiene como objetivo aplicar el TAd a un actuador *compliant*: el MACCEPA (de sus siglas en inglés, *mechanically adjustable compliance and controllable equilibrium position actuator*). El MACCEPA es un actuador basado en un elemento elástico en serie, cuya pre-compresión puede variarse, ofreciendo distintos grados de rigidez. La ventaja de este actuador es que permite aplicar un control de par sin necesidad de un complejo sensor de par, conociendo la constante del elemento elástico y las posiciones del motor y del ángulo articular del sujeto. En el estudio, se presenta adaptación del TAd al MACCEPA, en el banco de pruebas, mostrando que, mediante este algoritmo, y sin modificar la pre-compresión del elemento elástico, se puede modular la rigidez del actuador tanto en condiciones estáticas como dinámicas, demostrando que el control puede adaptarse a las capacidades del sujeto, de manera automática y autónoma.

El tercer estudio extiende los resultados a sujetos sobre la cinta de marcha, mostrando que el algoritmo permite absorber las desviaciones que pueda tener el sujeto sobre la trayectoria impuesta por el control del robot.

Estos estudios han demostrado el uso del TAd con un control de posición. Para el desarrollo de la herramienta, se prueba también su uso con un control de par, para poder modular la magnitud del par aplicado.

El siguiente capítulo muestra dos protocolos aplicables a la fase T2, justo antes de empezar un entrenamiento de marcha libre. Se utiliza la misma herramienta robótica, variando el ángulo en que reposa la pierna del sujeto, para poder ser utilizado en bipedestación. Este estudio tiene como objetivo explorar los controladores de par con la herramienta de rehabilitación robótica propuesta.

El primero de los entrenamientos consiste en que el robot aplica un par negativo (hacia el suelo), durante el tiempo equivalente a la fase de balanceo, para forzar a que el sujeto haga un par de dorsiflexion superior al habitual para poder seguir una trayectoria angular de tobillo natural en caminata. Al final del entrenamiento, durante el 15 - 20 % final del tiempo, se quita el par negativo. Se observa que los sujetos tienen una dorsiflexión mayor al quitar el efecto, así como una activación menor de los músculos dorsiflexores (en ausencia de la fuerza a compensar), y tienden a normalizar los patrones a lo largo del tiempo. Observamos también que cuando se deja de aplicar el par, hay una tendencia a anticiparse al efectuar el pico máximo de dorsiflexión en la fase de balanceo, tendencia que va desapareciendo con el tiempo.

En el segundo entrenamiento, el robot ejerce un par positivo, similar al ejercido por el suelo en la fase de apoyo, pero de una magnitud inferior, durante todo el entrenamiento. Se observa una activación inferior en el gastrocnemio medial (músculo plantarflexor) que durante una caminata normal sobre suelo. Esto indica que la fuerza reducida efectuada por el robot es similar a una caminata con un sistema de suspensión del peso.

A continuación, se presenta el desarrollo de la realimentación visual a modo de videojuego. El juego consiste en un autogiro cuya posición en el eje vertical puede modificarse por medio de la dorsi y plantarflexión del tobillo instrumentado (el eje horizontal avanza de manera automática). El objetivo es recoger las botellas de gasolina que aparecen en la pantalla, siguiendo la trayectoria óptima entre botellas.

El siguiente estudio, cuyo objetivo es demostrar la viabilidad de uso de la herramienta integrada por tobillo robótico fijado a la plataforma y el videojuego de rehabilitación, previo a aplicar el TAd, expone que aplicando un entrenamiento sin modular de ninguna manera, y modulando de manera progresiva y con una regla simple, el máximo par aplicado por el robot, se promueve aprendizaje en sujetos sanos, siendo mayor con los enfoques modulados.

Una vez probada la viabilidad de la herramienta para fomentar el aprendizaje motor en sujetos sanos, se presenta la adaptación del TAd al MACCEPA, esta vez controlado en par, dando lugar a lo que hemos bautizado como retroalimentación adaptativa háptica (HAF, de sus siglas en inglés, *haptic adaptive feedback*). Este paradigma hace uso del rendimiento en la tarea para modular la máxima amplitud del par efectuado por el robot en cada momento en función de las capacidades del sujeto. De esta manera, se mantiene el concepto de reto, sin sobrepasar en exceso las capacidades del sujeto, y adecuándose según se producen mejoras en la ejecución de la tarea.

El último estudio presentado, correspondiente a la fase de desarrollo, presenta los resultados a la hora de probar la viabilidad del protocolo final con un sujeto sano. A lo largo de cinco días consecutivos, el sujeto recibió el entrenamiento con el tobillo robótico consistente en jugar al videojuego diseñado para fomentar el aprendizaje motor. Se observó que el sujeto aprendía a lo largo de los días, mostrando reducción significativa en el error a la hora de seguir la mejor trayectoria entre botellas, así como aumento significativo en la puntuación, entendida como número de botellas recogidas. El estudio demuestra que el protocolo es capaz de generar aprendizaje en un sujeto sano.

El siguiente capítulo muestra una ampliación del estudio previo a una muestra de diez sujetos sanos, aplicable a la fase de terapia T1. Los sujetos entrenaron a lo largo de tres días consecutivos. Además, se registró la excitabilidad corticoespinal por medio de TMS, enfocado en el tibial anterior, antes de empezar el entrenamiento el primer día, justo después del entrenamiento del tercer (y último) día, media hora después para ver si los efectos se mantenían con el tiempo, y 24 horas después, para ver efectos a largo plazo. Se observó, a lo largo de los días, un incremento tanto en puntuación como en error. Así mismo, se obtuvo un incremento significativo en la excitabilidad corticoespinal del tibial anterior, pero no así de los otros dos músculos registrados: sóleo (como músculo involucrado en la tarea) y recto femoral (como músculo proximal, y, por tanto, no involucrado en la tarea de dorsi/plantarflexión). La falta de cambios significativos en el sóleo puede deberse a que al ser un músculo cuya acción es a favor de la gravedad, se haya visto menos potenciado. Otra posible razón es que, debido a que el tibial anterior recibe una mayor densidad de proyecciones corticoespinales que el resto de músculos del miembro inferior, necesite una intensidad inferior para ser reclutado en comparación con el sóleo.

Se extendió este estudio con un caso de estudio con un sujeto patológico para probar la viabilidad de aplicación del protocolo con pacientes. Para ello, se modificó el par realizado por el robot para que sólo forzase dorsiflexión, evitando que el paciente tuviera que compensar un movimiento del robot hacia abajo, centrado en entrenar los músculos dorsiflexores. Se observó un incremento significativo en la puntuación en la tarea del videojuego, así como un decremento significativo del error, a lo largo de los cinco días de experimento. En el caso del paciente se registraron también escalas clínicas, observando mejoras en resistencia, velocidad, distancia recorrida y tiempo de transición a bipedestación. Por último, también se registró el rango de movimiento y velocidad de dorsi/plantarflexión por medio de un test diseñado ad-hoc, en el que se pidió al sujeto que moviera el pie arriba y abajo lo más rápido posible para tocar con una bolita los extremos verticales de la pantalla. Se observó una mejora en esta métrica a lo largo del tratamiento. Aunque se ven mejoras, no puede extrapolarse este resultado a la población de sujetos patológicos, así como no se pueden aislar los efectos del juego del resto de la terapia diaria del paciente; pero se concluye que es un entrenamiento viable para su uso en entornos clínicos.

Technical abstract

THIS doctoral thesis presents, after reviewing human gait, the main pathologies and conditions that affect it, and the different rehabilitation approaches with the corresponding neurophysiological implications, the research journey that leads to the development of the rehabilitation robotic tool, and the therapies that have been designed, within the framework of the European projects BioMot: *Smart Wearable Robots with Bioinspired Sensory-Motor Skills* and HANK: *European advanced exoskeleton for rehabilitation of Acquired Brain Damage (ABD) and/or spinal cord injury's patients*, and tested under the umbrella of the European project ASTONISH: *Advancing Smart Optical Imaging and Sensing for Health* and the national project ASSOCIATE: *A comprehensive and wearable robotics based approach to the rehabilitation and assistance to people with stroke and spinal cord injury.*

Initially human gait is presented, characterizing it according to its stance and swing phases, and the spatiotemporal, kinetic and kinematic parameters, without neglecting the physiological parameters; followed by a review of the main pathologies or conditions that affect human gait: spinal cord injury, cerebral palsy, traumatic brain injury, neuromuscular impairments, osteoarticular diseases, aging, and stroke or cerebrovascular accident. Next, the robotic tool that is developed in this thesis is framed in the context of rehabilitation for stroke, based on its use in this widespread pathology, as it affects 13.7 million people every year, since there are about 80 million survivors, affecting all age ranges. In addition, 80 % of people affected by a stroke find also compromised their motor abilities, motivating the need to develop tools focused on the rehabilitation and recovery, as far as possible, of the independence lost due to the disease, with gait as a fundamental component of that independence.

After reviewing gait and the characteristics of the pathology, an explanatory review is given for the three phases of therapy for gait rehabilitation: T1) preparatory training based on mobilization of the lower limb joints; T2) gait recovery; and T3) improvement of gait with the aim of recovering mobility for activities of daily living. This classification of the therapy phases is presented to frame the work of this thesis in phases T1 and T2.

Motor recovery is based on motor learning, and thus, I provide a brief introduction to it, exposing its relationship with neuroplasticity, and establishing that, in order to

enhance all types of learning, it is essential to establish a challenge, *i.e.*, an acceptable difficulty, not only making the training less monotonous, but also enhancing retention. Motor learning, like all kinds of learning, requires the occurrence of neural plasticity. Neural plasticity can be described by these four factors: 1) evolution of neuronal representation for movements that require skill, which were latent before the injury; and recruitment of healthy areas that were used before the injury occurred, when the difficulty of the task was greater; 2) greater excitability of neurons and more efficiency of synaptic connections; 3) morphological changes associated with long-term potentiation and depression (LTP and LTD) phenomena; and 4) adaptation of cortical, subcortical and spinal networks that still function to the learned movement. There are different non-invasive methods that allow the evaluation of neuroplastic changes (Hoffman reflex, F-wave, motor evoked potentials, etc.), and since in this thesis the motor evoked potentials (MEPs) have been assessed, transcranial magnetic stimulation (TMS) is presented as the technique used to evoke potentials in the motor cortex associated with the muscle or muscles whose excitability is being evaluated, collected by means of superficial electromyography. The TMS technique allows to observe changes in corticospinal excitability before and after a treatment that potentially induces motor learning, being able also to evaluate if these changes are related to the treatment, as well as allowing to observe if they are long-lasting.

In the literature review chapter, the differences between traditional rehabilitation approaches, and those robotic technology-aided are also introduced, showing that there is no clear winner in such a battle, but showing the advantage of robot-aided approaches, as they allow objectively measuring and help characterizing the recovery process. Once the robotic technology has been introduced as a rehabilitation technology, exoskeletons are presented as the most appropriate robotic technology involved in rehabilitative approaches for gait, and a review of the relevant existing devices, with their characteristics and limitations, is given to show the motivation of this work. The limitations presented by current devices are: they use pre-recorded patterns; they do not have visual feedback systems, or their feedback systems are too simple, not presenting the potential of a video game: entertainment and adherence to the treatment, allowing the difficulty to be modified. Some, on the other hand, are so complex that they demand a high cognitive effort for patients, or are even complex to configure and command, leading to the abandonment of the technology by both patients and therapists. In addition, most of them lack the ability to introduce randomness in the treatment, potentially leading to boredom of the patient, and ultimately abandonment of the therapy. Last but not least, the tasks are not adapted along the treatment to the capacities and the recovery of the subject.

Therefore, the tool proposed in this thesis consists of the integration of a robotic ankle fixed to a platform, with a visual feedback comprised of a video game designed to train movements in the sagittal plane of the ankle: dorsiflexion and plantarflexion; with the subject sitting. The tool is capable of generating controlled torque patterns that disturb the trajectory followed by the subject, increasing the difficulty to collect the items on the screen. In addition, the magnitude of these disturbances depends on the performance during the task, increasing the difficulty when the performance is rising, managing to impose a continuous challenge, enhancing the adherence to the treatment as well as its effectiveness to promote the retention of what has been learned.

After presenting the review of the literature, I present the development of the rehabilitation tool, describing the journey from the test of the control algorithms, to the development of the video game and design of the experimental protocol, through the adaptation of the control to the compliant actuator on which the tool is based, or tests first on a test bench and then with healthy subjects wearing the device.

The first study presents the application of a bioinspired algorithm for autonomous learning, used in bipeds (providing them with the ability to learn to walk without prior knowledge of the task nor the environment, only knowing some points of the angular trajectory), to a six degrees of freedom actuated exoskeleton, with rigid actuators, in the sagittal plane, corresponding to the three main joints of the lower limb, *i.e.*, hip, knee and ankle. This adaptation of the algorithm allows to modulate the rigidity of a rigid actuator with a simple implementation. The term tacit adaptability (TAd) was coined to refer to this control strategy.

The second study I present aims to apply the TAd to a compliant actuator: the MACCEPA (mechanically adjustable compliance and controllable equilibrium position actuator). The MACCEPA is an actuator based on a series elastic element, whose pre-compression can be varied, offering different degrees of stiffness. The advantage of this actuator is that it allows to apply a torque control without the need for a complex torque sensor, knowing the constant of the elastic element and the positions of the motor and the subject joint angle. In the study, the adaptation of the TAd to the MACCEPA is presented, in the test bench, showing that, with this algorithm, and without modifying the pre-compression of the elastic element, the rigidity of the actuator can be modulated both in static and dynamic conditions, demonstrating that the control could be adapted to the capabilities of the subject, automatically and autonomously.

The third study extends the results to subjects on a treadmill, showing that the algorithm allows to absorb the deviations that the subject may have on the trajectory imposed by the controller of the robot.

These studies have demonstrated the use of TAd with a position controller. For the development of the tool, its use is also tested with a torque controller, in order to modulate the amplitude of the applied torque.

Then, the following chapter shows two protocols applicable to the T2 phase, just before starting free overground gait rehabilitation. The same robotic tool is used, varying the angle at which the subject's leg rests, to be used standing up. This study aims to explore the application of torque controllers to the rehabilitation robotic tool.

In the first training, the robot applies a torque downwards, during the time equivalent to the swing phase, to force the subject to make a higher dorsiflexion torque to be able to follow a natural ankle angular trajectory profile. At the end of the training, during the final 15-20 % of time, the torque is removed. It is observed that the subjects have a greater dorsiflexion when the effect is removed, as well as a minor activation of the dorsiflexor muscles (in the absence of the force to be compensated), and tend to normalize the patterns over time. We also observe that when the torque downwards is removed, there is a trend to anticipate the maximum dorsiflexion peak angle in the swing phase, a trend that tends to disappear over time.

In the second training, the robot exerts a torque upwards, similar to that exerted by the ground in the stance phase (ground reaction force), but at a lower magnitude, throughout the training. A lower activation is observed in the gastrocnemius medialis (plantarflexor muscle) than during a free walking over ground. This indicates that the reduced force made by the robot is similar to that experienced when wearing a body weight support.

Next, the development of the visual feedback based on a video game is presented. The game consists of a gyrocopter whose position on the vertical axis can be modified by means of the dorsi and plantarflexion of the instrumented ankle (the horizontal axis advances automatically). The aim of the game is to collect the gas bottles that appear on the screen, following the optimal trajectory between bottles.

The following study, whose objective is to demonstrate the feasibility of using the tool integrated by the robotic ankle fixed to the platform and the rehabilitation video game, prior to applying the TAd, exposes that applying a training without modulating, and modulating progressively and with a simple rule, the maximum torque applied by the robot, learning is promoted in healthy subjects, being greater the learning with the modulated approaches.

Once the viability of the tool to promote motor learning in healthy subjects has been proven, the adaptation of TAd to MACCEPA, with a torque controller, is presented, giving rise to what we have dubbed as haptic adaptive feedback (HAF). This paradigm makes use of the performance in the task to modulate the maximum amplitude of the torque exerted by the robot, depending on the capabilities of the subject. In this way, the concept of challenge is maintained, without excessively exceeding the subject's capabilities, and adapting to the improvements in the execution of the task.

The last study I present, corresponding to the development phase, presents the results when testing the feasibility of the final protocol with a healthy individual. For five consecutive days, the subject received a training with the robotic ankle consisting of playing the video game designed to encourage motor learning. We observed that the subject learned throughout the days, showing a significant reduction in the error when following the best trajectory between bottles, as well as a significant increase in the score, understood as the number of collected bottles. The study shows that the protocol is capable of generating learning in a healthy subject.

The following chapter shows an extension of the previous study to a sample of ten healthy subjects, applicable to the T1 therapy phase. The subjects trained for three consecutive days. In addition, corticospinal excitability was recorded by means of TMS, focused on the tibialis anterior muscle, before starting the training on the first day, just after the training on the third (and last) day, 30 minutes later to see if the effects were maintained along time (LTP-like), and 24 hours after, to see long-lasting effects. An increase in both score and error was observed throughout the days. Likewise, a significant increase in the corticospinal excitability of the tibialis anterior was obtained, but not in the other two registered muscles: soleus (as a muscle involved in the task) and rectus femoris (as a proximal muscle, and, therefore, not involved in the task of dorsi/plantarflexion). The lack of significant changes in the soleus may be due to the fact that being a muscle whose action is in favor of gravity, it has been less potentiated. Another possible reason is that, because the tibialis anterior receives a higher density of corticospinal projections than the rest of the lower limb muscles, it needs a lower intensity to be recruited compared to the soleus.

We extended this study in a case study with a pathological subject to test the feasibility of applying the protocol with patients. To do this, we modified the torque profile exerted by the robot so that it only forced dorsiflexion, preventing the patient from having to compensate for a movement of the robot downwards, focusing on training the dorsiflexor muscles. We observed a significant increase in the score in the task of the video game, as well as a significant decrease in the error, throughout the five days of the experiment. In the case of the patient, clinical scales were also recorded, observing improvements in resistance, speed, distance and transition time to standing position. Finally, the range of motion and speed of dorsi/plantarflexion were also recorded by means of an ad-hoc designed test, in which the subject was asked to move the foot up and down as quickly as possible to vertically move an onscreen ball to the limits of the screen. These metrics also shown improvements throughout the treatment. Nonetheless, these positive results cannot be extrapolated to the population of pathological subjects, as the effects of our training cannot be isolated from the rest of the patient's daily therapy; but it is concluded that it is a viable training for use in clinical scenarios.

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Introduction

Motivation of this thesis

Although current rehabilitation technology has incredibly advanced in the last years, so-called intelligent machines are today far from the flexibility found in the real-time adaptability of humans when confronted with changes in environmental and task constraints. The majority of current gait rehabilitation tools use prerecorded patterns from healthy users, with some studies in the line of adapting them to the patient characteristics (height, physiological measurements, fitness) [Colombo et al., 2000, Aoyagi et al., 2007, Wisneski and Johnson, 2007, Montagner et al., 2007, Bharadwaj et al., 2005]. There are a number of devices that present remarkable tools for stroke rehabilitation [Zhang et al., 2013, Basaha et al., 2017] (this state of the art analysis is presented in section 1.3.5), but we have identified some lacks on their designs or protocols, that we will use as the starting point for the development of the work presented in this thesis: some lack a visual feedback interface, or have one that lacks the potential of a more elaborate video game: promote active participation and engagement, and thus, adherence to the therapy. Some of them are so complex that lead to high cognitive a time demands from the clinicians, potentially leading to technology abandonment. This complexity also affects the task and thus the instructions given to the patient, stressing the need of having simple, functional and goal-oriented tasks. Furthermore, most of them lack randomness on the treatment, which can promote boredom and thus therapy abandonment from the patient's side, as the task may get unchallenging. Last but not least, the tasks lack adaptability to the internal metrics of the training.

Background

Human locomotion is the result of a two-way interaction between the neural networks, in both the brain and the spinal cord, and the mechanical periphery of the body. It includes starting, stopping, changing speed and direction. We constantly (consciously or unconsciously) use our neuromusculoskeletal system to interact with the environment.

Stable interaction, *e.g.* locomotion, is thus produced by the interplay between the neural (cortical and subcortical) and the musculoskeletal systems.

Stroke is a neurological condition that usually leads to an irreversible damage of brain structures. Stroke affects each year around 13.7 million people worldwide, being the second leading cause of disability [World Stroke Organization, 2018b]. As a consequence of brain lesions, stroke patients usually present motor impairments, which can range from mild to severe motor affectation. Daily living activities (DLAs), and consequently, the independence and the quality of life of the stroke survivors, are severely affected; therefore, rehabilitation of motor function is of paramount importance. Among all, the human motor function that provides more independence, and therefore limits more patients' quality of life when absent, is gait.

The main goal of post-stroke motor rehabilitation is to help patients recover from motor impairment and improve functional activities and quality of life. Typically, stroke patients are assisted by a caregiver. However, caregivers' aid usually will not overcome the low independence of patients nor the low self-esteem associated to reduced autonomy, which might lead patients into a spiral of negative feelings. For these situations, palliative alternatives such as surgical interventions and pharmacological and physiotherapeutic rehabilitation treatments arise as potential alternatives. Likewise, this is where technological advances and the convergence of multidisciplinary teams to achieve an improvement in their quality of life come into play.

Conventional motor rehabilitation focuses on training specific movements to re-acquire independence in DLAs. In fact, it has been seen that after local brain cortex tissue damage, rehabilitative training can produce a reorganization to some extent on the adjacent intact cortex [Nudo et al., 1996]. The underlying process that explains this reorganization after motor rehabilitation is motor learning (that is a form of plasticity [Mawase et al., 2017]): the central nervous system is able to adapt itself as a response to changes. The cortical reorganization or plasticity is induced in the first phases of rehabilitation by passive movements manually performed by therapists or more recently by robotic devices during motor training, using afferent pathways to activate the central nervous system. These findings suggest that undamaged motor cortex might play an important role in motor recovery of stroke patients, and it is important to note that motor recovery after brain injury is a form of motor learning [Krakauer, 2015] and functional recovery, mainly by means of optimizing sensorimotor performance in functional actions. Neuroplasticity is the mechanism behind the learning processes, and thus behind functional skills, so therapies should be designed to maximize optimal plastic changes [Aqueveque et al., 2017]. One important factor is that there seems to exist a direct relationship between impairment and function: for example, gait function is correlated to lower-limb impairment [Langhorne et al., 2009]. However, the probability of recovering independent mobility is currently very low with available methods: at the time of dismissal from a neurorehabilitation hospital, about 50 % of patients with subacute stroke are confined to a wheelchair, whereas less than 15 % are able to walk indoors without assistance, less than 10 % are able to walk outdoors, and less than 5 % are able to climb stairs [Paolucci et al., 2008]. Hence, there is a need for more effective therapies, which might be achieved by exploiting new technologies [Iosa et al., 2013].

Conventional therapy to retrain gait typically consists of two main phases: T1- preparatory training based on joint mobilization; and T2- gait training [Belda-Lois et al., 2011]. In T1, the patient trains gait-oriented lower limb movements, which are performed with and without therapist intervention. The aim of this procedure is to control the evolution of spasticity and to strengthen the muscles and joints necessary for standing and walking, *i.e.*, ankle, knee, and hip. In T2, the patient participates in sessions of gait training, which can be assisted by a human therapist. In this phase, the patient trains motor coordination to re-learn and re-acquire a physiological gait pattern.

Robots are crucial in the rehabilitation field, in the sense that they help the physiotherapist to provide an objectively equal movement to the patient's limb while providing objective view into the performance and improvements of the patient. Next lines will provide a brief approximation of the main approaches in using robots and haptics in the rehabilitation field. Several authors have tested the error augmentation approach [Patton and Mussa-Ivaldi, 2004,Emken and Reinkensmeyer, 2005,Patton et al., 2006,Scheidt et al., 2001] to enhance motor learning. The nervous system learns forming the internal model of the dynamics of the environment via a process of error reduction. Emken and Reikensmeyer concluded that motor learning process can be accelerated by exploiting the error-based learning mechanism. They used the approach of perturbing the movement via a robotic device, to augment the error while the user was performing the task. Combined haptic error augmentation and visual feedback have provided better results than conventional direct training (pure joint mobilization), exploiting the idea of using the after-effects of a resistive force to help perform the user the desired trajectory task [Bittmann and Patton, 2017]. Reikensmeyer and Patton [Reinkensmeyer and Patton, 2009] suggest combining robotic guidance and error augmentation techniques, starting with guidance and gradually removing it and increasing error augmentation. Indeed, this increased difficulty paradigm may be related to plastic changes at the cortical level and thus to a motor learning mechanism [Perez et al., 2004].

Marchal-Crespo et al. [Marchal-Crespo et al., 2014] showed that random disturbances improved motor learning in the performance of a simple dorsi-plantarflexion task, because this variability may increase recovery by increasing the needed effort and attention into the task. Thus they performed a new study [Marchal-Crespo et al., 2017] showing that "challenge-based" controllers, in which guidance was given on the first stages of the recovery, and error augmentation on the next and last stages of the rehabilitation, were more beneficial for recovery, as the therapy adapted to the patients. In the error augmentation phase, increasing errors lead to beneficial after-effects on gait, as it rendered the exercise more difficult to be performed. This added intensity to the training and probably served as a stronger learning stimulus pushing the patients out of the "comfort zone" and encouraging exploration of the new motor tasks. But it is important not to provide too high perturbations to the movement so they can be discouraging [Turner et al., 2013].

Current gait rehabilitation tools suffer from the rigidity associated to the use of pre-recorded patterns from healthy users, with some studies trying to adapt these "healthy" patterns to the patients' characteristics (height, physiological measurements, fitness) [Colombo et al., 2000, Aoyagi et al., 2007, Wisneski and Johnson, 2007, Montagner et al., 2007, Bharadwaj et al., 2005]. This rigidity can be overcame by means of bioinspired controllers that try to adapt the rigid trajectories to the capabilities, interaction, or performance of the human. In this sense, promising results have been achieved using robots controlled by tacit learning (TL). Thus, tacit learning [Shimoda and Kimura, 2010, Shimoda et al., 2010, Matsubara et al., 2006, Liu et al., 2007, Gibson, 2014] is proposed as a way of promoting the adaptation of the wearable robot to the patient based on the performance on the task, aiming at providing a reliable interface between both agents and adapting the difficulty to enhance the power of the treatment.

Active participation, motivation and attention are key elements in therapy for a potentially successful motor rehabilitation [Cramer et al., 2011]. It is capital for the success of the therapy that the patient understands the exercise and the potential outcome, to keep the engagement and the attention, thus enhancing motivation [Cano-de-la-Cuerda et al., 2015]. Furthermore, if the patient lacks the capacity to understand how an exercise is executed correctly, little effect can be expected [Asín-Prieto et al., 2014a]. It is important to note that stroke patients' learning function may be compromised as the result of brain injury. Video games seem to be an effective tool and feedback alternative/complement for improving function and health after stroke [Asín-Prieto et al., 2014a], and enhancing motivation [Swanson and Whittinghill, 2015]. In the literature we can find that visual feedback through video games helps to improve the performance in specific tasks, even improving the results in comparison to real-task training [Todorov et al., 1997].

Indeed, this visual approach has been proven to improve robotic haptic guidance therapy scenarios [Liu et al., 2006]. Furthermore, the idea of these video games makes the implicit learning process transparent for the user, not being aware of what is being learned [Patton and Mussa-Ivaldi, 2004]. Video games seem to be effective for improving function and health after stroke, and enhance motivation [Swanson and Whittinghill, 2015].

Objectives

Considering, on the one hand, that lower-extremity motor impairment arisen after stroke affects the independence of the patients and, on the other hand, the potential rehabilitative benefits of novel elements for therapy (robots and video games), the present dissertation proposes the combined use of a robotic device and a video game together. The control of the integrated tool relies on adaptability based on the patient performance on the task during the execution of dorsi-plantarflexion movements with the objective of promoting recovery of gait function.

The loss or reduction of mobility is not only exclusive to stroke, since its aetiology is much wider: ageing, spinal cord injuries, traumatic brain injury, multiple sclerosis, cerebral palsy, among other diseases, may result in reduced mobility. Even though this dissertation focuses on the design of a novel paradigm to rehabilitate gait post-stroke, it is worth pointing out that, those conditions leading to total or partial loss of mobility and that are prone to be rehabilitated, might also benefit from similar rehabilitative processes to those herein proposed.

The **main objective** of this doctoral thesis is to develop and validate a novel robotic system for gait rehabilitation for late T1 phase (mainly mobilization), and early T2 phase (previous to real walking exercises). The proposed system combines the advantages of the robotic technology with the use of video games for increased adherence to the therapy; relying on the performance of the patient for the tuning of the difficulty of the task via the adaptation of the control of the robot. The main objective in T1 phase is to challenge the patient as the performance improves, raising the difficulty according to performance on the task. The main objective of T2 phase therapy is to provoke relevant after-effects beneficial for the condition of the patient.

Explicitly, the following partial objectives are framed within this doctoral thesis:

1. To identify the current challenges for the robotic therapy aided by video games applied to gait rehabilitation; understand the pathologies that may benefit from this type of therapy focused on stroke.
2. To develop the rehabilitation tool consisting of a motorized ankle foot orthosis (MAFO) based on a compliant actuator (MACCEPA [Moltedo et al., 2016]) and a video game. For this,
   - we start exploring the implementation of the tacit learning bioinspired control algorithm, designed for bipeds, on rigid exoskeletons.
   - And then, we design and test the robotic tool and the visual paradigm that accompanies it, with classical torque control.

3. To design, implement and validate a torque controlled robotic tool and a therapy for early T2 phases of rehabilitation. Taking the tool from previous partial objective, we design the intervention for gait-like in standing rehabilitation tasks, thus being relevant for early T2 rehabilitation, where gait tasks are performed, so this protocol provides training for drop-foot and ground reaction force (GRF) simulation. We validate it with healthy subjects.

4. To design, implement and validate an adaptive control robotic tool and a therapy for late T1 phases of rehabilitation. Taking the tool from partial objective 2, we design the intervention for motor control learning in tasks of ankle joint mobilization, thus being relevant for late T1 rehabilitation, where mobilization is performed, but functional motor control is needed for the transition to T2, *i.e.* gait tasks. We validate it with healthy subjects, and carry out a pilot study with one stroke patient.

Thesis organization

Figure 1 depicts the roadmap to address these objectives. The *literature review* is an iterative process that feeds all the studies and developments on this dissertation, and is presented on **chapter 1**. The exploration of the *adaptive bioinspired control* on **chapter 2** was carried out to investigate the influence of this type of controller in a robotic therapy on the subjects with the available robotic tool by that moment: the H2 exoskeleton [Canela et al., 2013,Bortole and Pons, 2013,Bortole et al., 2015], and further developed and investigated on the testbench with the compliant MACCEPA actuator. **Chapter 4** presents the development and preliminary validation of the *rehabilitation tool* combining the robot and the video game. The design and implementation of the robotic tool and protocol for the phases T2 and T1 of the therapy are presented in **chapters 3 and 5**, respectively.

Thus, to fulfill the thesis' objectives, these are the chapters on this dissertation:

- Chapter 1: **Literature review** of the robotic therapy aided by video games applied to gait rehabilitation; together with an insight of the pathologies that can benefit from the rehabilitation tool (with emphasis on stroke).
- Chapter 2: **Exploration** of the technology prior to developing the rehabilitation tool. First, we present the implementation of the translation of the bioinspired controller from bipeds to rigid exoskeletons. I present also the first implementation of this bioinspired controller on MACCEPA for a position controller.
- Chapter 3: **Modulation of muscle activity applying novel force paradigms**. This chapter presents the specific design and implementation of the rehabilitation

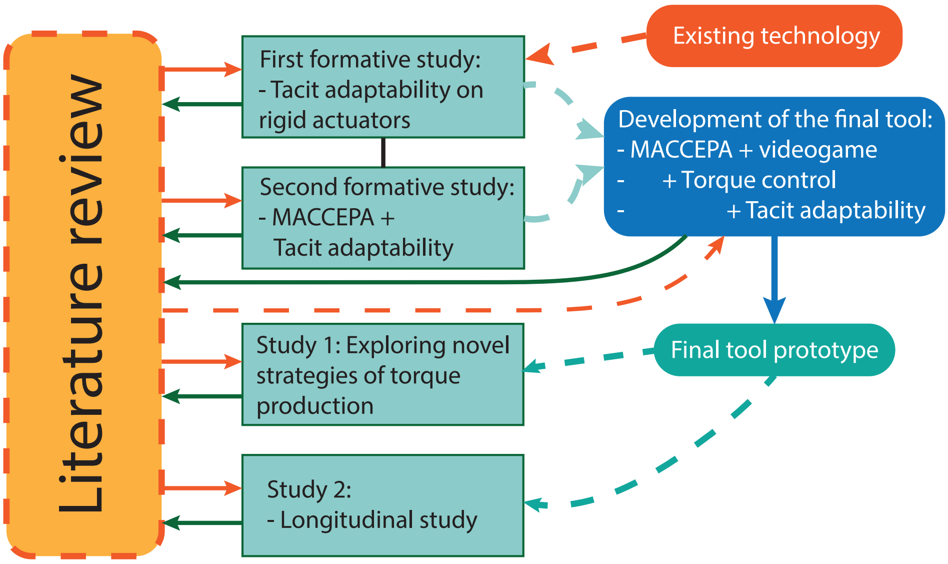


FIGURE 1: Roadmap of this thesis.

tool and protocol for a therapy for early T2 phase of rehabilitation (preparative exercises for gait), and results of trials with healthy subjects, where we explored the application of torque with the proposed rehabilitation tool.

- Chapter 4: **Development** of the rehabilitation robotic tool. I show the concrete development of the rehabilitation tool, including the proposed feedback paradigms and the visual interface, before presenting the results on the first study with a healthy subject.

- Chapter 5: **Evaluation of haptic adaptive feedback to promote motor learning**. This chapter presents the specific design and implementation of the rehabilitation tool and protocol for a therapy for late T1 phase of rehabilitation (mobilization), the results of trials with healthy subjects, and a pilot study with a stroke patient.

- Chapter 6: **Conclusions**.

Chapter 1

Literature review

MOBILITY is one of the main functions on human beings, and not only permits locomotion to perform daily living activities, but also to interact with the surrounding environment, either physically and socially in all the facets of life. Hence, the impact of the partial or total loss of mobility is huge as it conditions a person's entire life and forces them to adapt to this new reality. In children or youngsters the impact is even greater, since it also affects the formation of its own personality due to being in a phase of physical and psychological development.

In general, awareness of the problems that disability entails in society is lacking [World Health Organization, 2011]. In the first place, the truth is that motor deficits cause specific mobility problems, that affect postural control or manipulation, affecting also to routine movements associated with the locomotor system: standing up, sitting, or standing position, requiring in most cases the use for external support. Second, there are physiological problems related to long inactivity periods: muscle mass loss; circulatory, digestive, respiratory, renal and urinary problems; pressure sores; muscular and joint contractures; etc. In the third place, it is worth mentioning other important life aspects such as sexuality, personal relationships and social inclusion; and, therefore, the huge psychological impact that the problem supposes. The self-esteem of these people is seriously affected on most cases, since they are not able or have difficulties to take part on leisure or social activities, or have more difficulties when getting a job. And last but not least, there are high expenses derived from their dependence situation.

In recent years, the efforts on the progress in the elimination of architectural barriers have greatly increased, although it is still insufficient. Article 20 of the International "Convention on the Rights of Persons with Disabilities (CRPD)" addresses this need for personal mobility. In it, "States Parties shall take effective measures to ensure personal mobility with the greatest possible independence for persons with disabilities" [United Nations Enable, 2016]. These measures include the following:

“a) Facilitating the personal mobility of persons with disabilities in the manner and at the time of their choice, and at affordable cost;

b) Facilitating access by persons with disabilities to quality mobility aids, devices, assistive technologies and forms of live assistance and intermediaries, including by making them available at affordable cost;

c) Providing training in mobility skills to persons with disabilities and to specialist staff working with persons with disabilities;

d) Encouraging entities that produce mobility aids, devices and assistive technologies to take into account all aspects of mobility for persons with disabilities.”

The description of human gait is exposed hereunder, and after it, the main pathologies that affect it are presented.

1.1 Human gait

Humans start to acquire the ability of locomotion around the first year or life [Sheridan, 1975]. At this stage, gait is unsafe, unstable, wobbly, very irregular and lacks of harmony and coordination [Vázquez, 2005]. It is a learning process that involves the development of muscle strength and the coordinated action of the involved organic elements. During this period, bipedal position is achieved, as it is the stable position and basic to start walking. Human beings learn autonomously and experimentally, thus achieving their own characteristic gait, which can be described by means of a set of parameters that define a gait pattern, common for all human beings.

Gait is a sequence of events where different systems of the human body are involved, and it can be simplified, (focusing on the lower limbs) in the following sequence of steps, depicted on Figure 1.1, according to Vaughan et al. [Vaughan et al., 1999]:

1. Registration and activation of the gait command in the central nervous system
2. Transmission of the gait signals to the peripheral nervous system
3. Contraction of muscles that develop tension
4. Generation of forces at, and moments across, synovial joints
5. Regulation of the joint forces and moments by the rigid skeletal segments based on their anthropometry
6. Displacement (*i.e.*, movement) of the segments in a manner that is recognized as functional gait

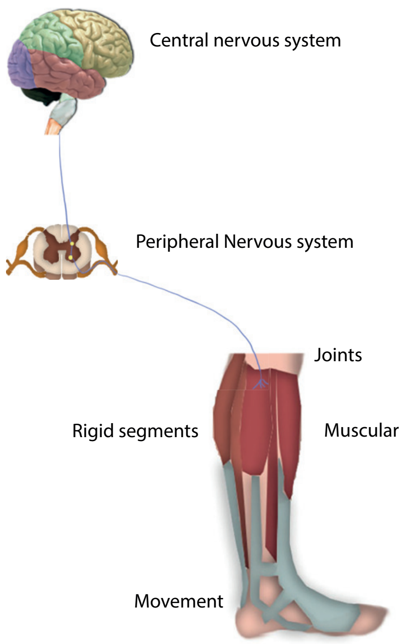


FIGURE 1.1: Cascade of events for the generation of gait.

7. Generation of ground reaction forces

This sequence supposes a great simplification of the biological process of gait, as it also has an important contribution from the upper extremities and the trunk, in terms of dynamic equilibrium and towards the optimization of energy efficiency. From a conceptual point of view, human gait is defined as a series of alternating and dynamic movements, both of the extremities and the trunk, which determine a forward displacement of the centre of gravity [Dávila and de la Cruz Márquez, 1988]. To walk, one leg is risen and moved forward, while the other leg is the supporting one. In this process, the centre of gravity moves laterally, to keep balance, and vertically against gravity, to increase energy efficiency. From an anatomical point of view, gait can be defined by three specific planes, called cardinal planes of the body (Figure 1.2), which have their origin in its centre of gravity: the sagittal plane (or anteroposterior), the coronal (or frontal), and the transverse (or horizontal) plane. During locomotion, most of the movements take place in the sagittal plane.

The set of events that take place during locomotion is known as a gait cycle.

1.1.1 Gait cycle

Gait cycle begins when one foot contacts (initial contact, IC) the ground and ends when the next IC of **the same foot** occurs. In this process, we distinguish two phases: stance and swing (Figure 1.3). In stance, the foot is in contact with the ground, while in swing the foot swings forward without any contact with the ground. The stance phase

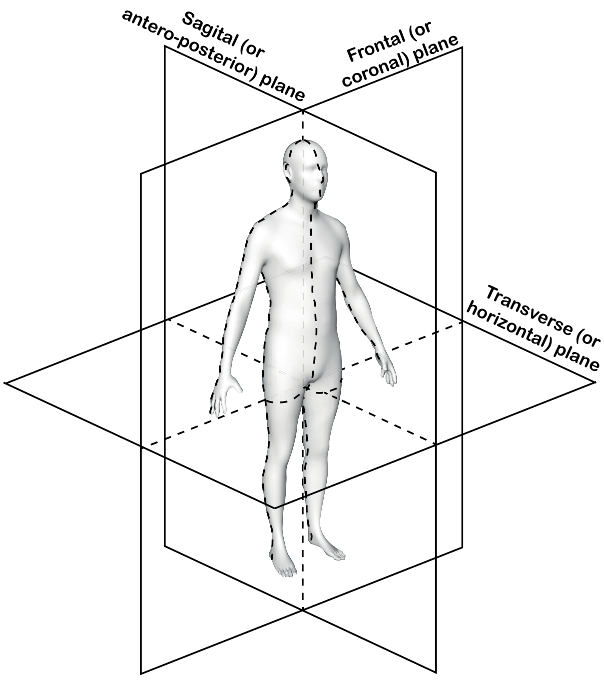


FIGURE 1.2: Cardinal planes of the human body.

represents 60 % of the cycle, while the remaining 40 % corresponds to the swing phase. During the process, there is also the double-support phase, in which both legs are in contact with the ground, and which represents 20 % of the cycle.

Human gait cycle can be described by a set of spatiotemporal, kinematic, kinetic (forces and moments) and physiological parameters. In most of the gait studies, at least the spatiotemporal and kinematic parameters are analyzed, in order to study the progress of the patient's gait.

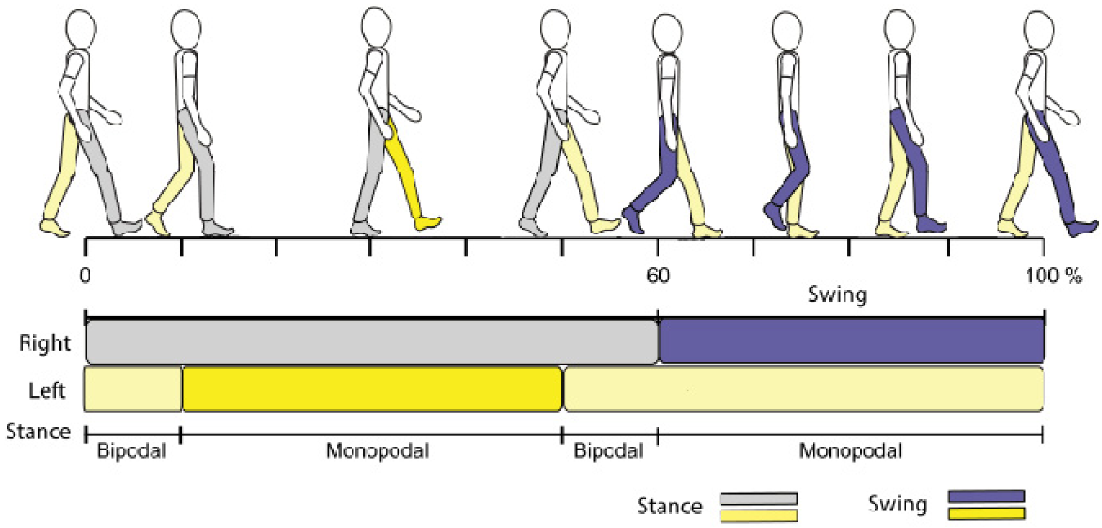


FIGURE 1.3: Description of the gait cycle in its phases of stance and swing with detail of the monopodal and bipodal supports.

1.1.2 Gait variables

One way to characterize and establish the symbiotic relations between humans and wearable robots (WRs) is to synthesize the walking behaviour and adaptation. In this characterization we set a theoretical framework to understand walking by means of a collection of the gait variables involved in this work.

1.1.2.1 Spatiotemporal parameters

The spatiotemporal parameters are the most frequently analyzed variables in gait studies, since they do not require high cost equipment and allow a direct evaluation of the evolution. According to Robinson and Smidt [Robinson and Smidt, 1981], they provide the most simple and objective evaluation tool. Main spatiotemporal parameters are:

- Step length: Linear distance in the plane of progression (sagittal) between contralateral ICs.
- Width of the step: Lateral separation between both feet measured from the heels.
- Stride length: Distance traveled between two consecutive ICs of the same foot.
- Cadence: Number of steps in a time interval, commonly, number of steps per minute.
- Travel speed: Distance traveled in an elapsed time.

1.1.2.2 Gait kinematics

Gait kinematics study the movement of the body. David Winter, considered the father of modern biomechanics [Winter, 2009], presented a study with healthy subjects, where he extracted the typical biomechanical gait patterns for the six joints: hips, knees and ankles (see Figure 1.4 for the sagittal plane).

1.1.2.3 Gait kinetics

Gait kinetics study the external and internal forces that occur during gait process. The main parameter that is studied is ground reaction force (GRF), which is equal to the downward impulse of the foot against ground, but in the opposite direction. Figure 1.5 shows the characteristic profile of this force for a normal pattern.

There is a rapid increase in the reaction force, due to the right initial contact, and the transfer of weight from the left side of the body towards the right, with its respective

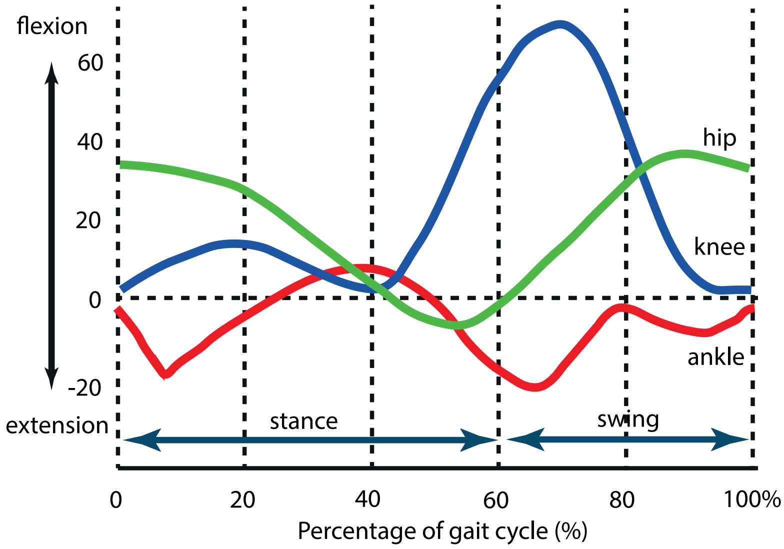


FIGURE 1.4: Range of motion in the sagittal plane of the lower limb during a gait cycle. Adapted from [Winter, 2009].

acceleration. Then, there is an overshoot related to the load response phase, since the transferred weight is damped. Once in mid stance, reaction force decreases for the right leg, to rise again in an overshoot related to the push off, prior to the foot taking off. Finally, during swing there are no ground reaction forces, since the leg is in the air.

1.1.2.4 Physiological parameters

Up to now, the parameters associated with joint mechanics have been presented, but there are physiological parameters of great interest associated with gait. Among them are the electromyography, the energy consumption or the cardiac frequency. The analysis of these parameters provides relevant information about a person's physiological state, which complements the biomechanical analysis.

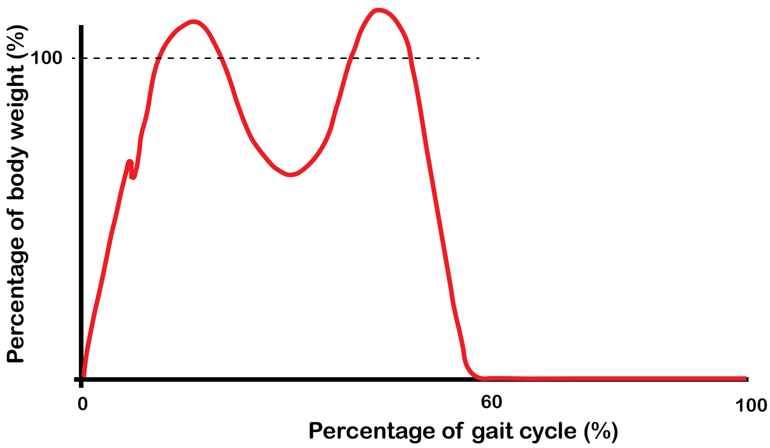


FIGURE 1.5: Ground reaction force for a gait cycle, adapted from [Perry et al., 1992].

Electromyography is responsible for recording the electrical activity produced by the muscles in response to nerve stimulation. This measurement provides information to determine which muscle group is responsible for a contraction, if antagonistic activity occurs (co-contraction), information on the pattern of muscular activity or detection of muscle fatigue. Said information can be used as a diagnosis of neurological and neuromuscular problems.

Gait is an efficient process that tends to minimize the required energy cost. Therefore, the measurement of the metabolic consumption is important since it allows to quantify its physiological state, to study its evolution and possible physiological disabilities. To characterize this consumption, certain measures are used that are usually normalized with the weight of the individual and certain environmental conditions to be contrasted between each other, such as the consumption or the cost of oxygen and CO_2. Finally, these data are usually complemented with the measurement of the cardiac rhythm.

1.2 Abnormal gait: main pathologies

The loss or reduction of mobility is one of the main problems associated with ageing. However, this motor deficit is not only exclusive to the elderly, but its aetiology is much wider. Cerebrovascular accidents, spinal cord injuries, injuries, multiple sclerosis, cerebral palsy, among other aetiologies, lead in most cases to partial or total loss of mobility and generate a motor disability. Depending on the degree of affectation, the person is limited in his daily life.

Human walking process starts in the central nervous system (CNS) with the generation of so-called motor patterns. Specifically, these patterns are generated by neuronal networks known as "Central Patterns Generators" (CPG) [MacKay-Lyons, 2002, Dimitrijevic et al., 1998], and are modulated by the excitations provided by the visual, vestibular and somatosensory systems [Dietz, 2003]. These systems provide information such as, *e.g.*, the spatial position of the lower limbs, in order to maintain balance either in static situations or in gait. The peripheral nervous system (PNS) collects this information, interprets the sensory information and generates commands to the musculoskeletal system to ensure both the movement of the body and balance, so that the centre of mass remains always stable [Vaughan et al., 1999].

Gait process is, therefore, a set of complex interactions between several systems of the human body. Henceforth a compromised situation of any of them causes an alteration in locomotor system, modifying the gait patterns and even preventing it. Consequently, it usually leads to negative changes in muscle tone, and absence (palsy) or weakness (paresis) of voluntary movements. These alterations can affect only on one side of the body, both sides, only to part of the limbs, or to the four limbs... the higher the neurological-muscular damage, the greater the impact on the rest of the systems below the lesion.

There are several causes that can affect the locomotor system, and next lines non-exhaustively expose the most typical, with special emphasis on stroke (main focus of the therapies, protocols and device that will be presented in this dissertation), although all of them might also benefit from similar rehabilitative processes to those applicable to stroke.

1.2.1 Spinal cord injury

Spinal cord injury (SCI) is understood as any temporary or permanent spinal cord alteration that can "cause changes in movement, sensation, or function below the level of the injury" [Asín-Prieto et al., 2016b]. The prevalence of spinal cord injury varies according to the features of the population and the aetiological diversity. In Spain, approximately 1,000 new cases of spinal cord injury per year occur, *i.e.* an incidence rate of 26-27 injuries per million inhabitants each year [Huete et al., 2012], and the lesion origin can be classified as:

- Traumatic, due to for example to traffic, work or sport accidents. Around 33 % of cases of spinal cord injury are of traumatic type.
- Non traumatic, may be congenital or acquired via infectious, vascular, autoimmune, inflammatory, etc., diseases. It represents 67 % of cases of spinal cord injury.

SCI is defined primarily by the vertebral level at which the damage occurs, as well as by the degree of preservation of the motor function and sensitivity below the level of injury.

1.2.2 Cerebral Palsy

Cerebral palsy (CP) is defined as a "a disorder of movement and posture due to a defect or lesion of the immature brain" [Bax et al., 2005]. CP can occur both in the prenatal and in the perinatal period, and even in the postnatal period. Currently, the incidence in developed countries is around two cases per thousand births and year [Odding et al., 2006]. In Spain around 0.25 % people have been affected [CONFEDERACIÓN ASPACE, 2014].

Motor disorders associated with CP, such as alterations in muscle tone, posture and movement, usually appear with variations in sensation, cognition, communication, perception, and, in some cases, behaviour.

1.2.3 Traumatic Brain Injury

Traumatic Brain Injury (TBI) is described as the brain lesion, from non-congenite or degenerative nature, caused by a physical external force that can provoke an injury with consciousness affection, and potentially entailing alterations on the cognitive, physical and/or behavioural abilities [Campbell, 2000]. The consequences can be temporary or permanent, and can cause partial or total disability with psychosocial disorders [Dawodu, 2013]. According to the Ombudsman's Report, it is estimated that the incidence of TBI in Spain is of 200 new cases per 100,000 inhabitants, of which 10 % are serious, 10 % moderate, and the remaining 80 % mild [Defensor del Pueblo, España, 2005].

Brain damage does not always immediately after the impact (primary injury), but may also appear later (secondary injury). The primary injury is caused directly by the contusion itself or the associated stroke, causing a loss of consciousness and orientation, whereas the secondary one is the result of the local complications and alterations produced in the organism, like the increase of pressure in the skull, respiratory failure, hypotension, intracranial hematoma, etc.

The sequelae of a TBI are of great diversity in the cognitive and behavioral field, and vary in their nature and severity depending on the extent and location of the affected brain area [Defensor del Pueblo, España, 2005].

1.2.4 Neuromuscular impairments

Neuromuscular diseases are a set of hereditary or acquired diseases that affect the nerves that control muscle fibres. Motor neurons are unable to communicate and activate the desired muscle group, so there is a progressive loss of muscle strength, and a degeneration of the muscles and nerves that control it. As a consequence, spasms, pain and joint problems may occur, as well as difficulty for breathing, chewing or holding the head upright. The clinical course of these these neuromuscular diseases may be intermittent, with outbreaks of activity and remission phases. However, some are lethal due to the progression of the disease or the associated complications. Thus, for example, myasthenia gravis causes weakness in the voluntary muscle groups, and this weakness increases with activity but improves with rest; and that can lead to a wide variety of symptoms such as facial paralysis, fatigue, difficulty for climbing stairs, lifting objects or getting up from a sitting position [López de Munain, 2006]. Myotonia, on the other hand, is characterized by the difficulty in muscle relaxation after a contraction. People with this disorder may have difficulty getting up from a sitting position, and present a stiff and clumsy gait.

1.2.5 Osteoarticular diseases

Osteoarticular diseases are those that affect bones and joints. They consist mainly on rheumatism, degenerative processes (such as osteoarthritis) or inflammatory (such as rheumatoid arthritis, polymyalgia rheumatism or gout) and non-articular processes (such as tendinitis, capsulitis). In general, they all have in common: functional limitations, deformities and pain.

Within the group of these processes, we find osteoporosis, which consists of a decrease in the bony mass, due to the body not being able to generate enough new bone to replace the one that is reabsorbed, leading to bone fragility. Thus, fractures are more likely to occur, being the most usual breaks those on hip, wrist or vertebrae. In general, these negative osteoarticular processes are intimately related to ageing. The prevalence of osteoporosis in women over 70 years old is 52 % [Balaguer and Olmos, 2005].

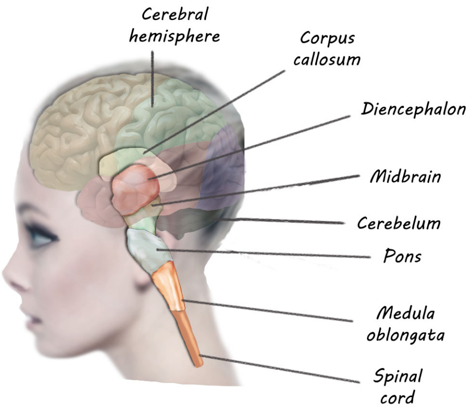
1.2.6 Ageing

Ageing usually leads to the appearance of pluripathologies with a tendency to chronicity and disability. Among the main pathologies related to ageing we find muscle weakness, joint alterations (such as osteoarthritis), neurological pathologies, and strokes; which, in addition, contribute to the increase of falls and frequently require the implantation of hip prosthesis. This type of population is characterized by a more rigid gait [Ducroquet et al., 1972], looking to increase stability and safety during gait by decreasing step length and speed [Lacuesta et al., 1993].

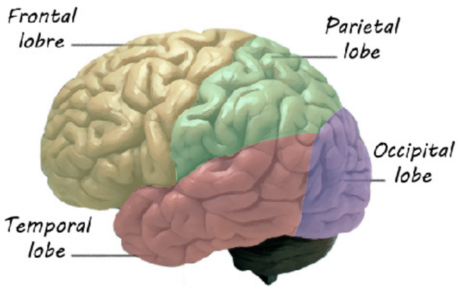
According to the report “Elderly people in Spain” [Vidal Domínguez et al., 2017], 72.2 % of elderly people declare mobility problems in far superior proportions than to other disabilities, *i.e.* more than 1.6 million people over the age of 65 have motor problems to some extend. This figure will increase in the next few years, since life expectancy is increasing. According to the Spanish National Institute of Statistics, currently those over 65 years old represent “only” 18.2 % and estimate that by 2064 will be 38.7 % of the population, *i.e.* 15.8 million people [Instituto Nacional de Estadística (INE), 2014].

1.2.7 Stroke

Cerebrovascular accidents (CVA) or **stroke** occur when there is a total or partial interruption of the blood supply, and thus also of nutrients and oxygen, in a part of the brain, due to that a blood vessel in said organ is obstructed (ischemic accident) or broken (haemorrhagic accident) [Sims and Muyderman, 2010]. The CNS is a very complex system, composed of two main parts: the spinal cord and the brain. It has a symmetrical structure divided in two sides. Focusing on the brain, it is formed by six structures (see Figure 1.6(a)): medulla oblongata, pons, cerebellum, midbrain, diencephalon, and the



(a) Main structures of the brain.



(b) The four lobes of the cerebral cortex.

FIGURE 1.6: Human central nervous system main components.

two cerebral hemispheres. The hemispheres are subdivided in four main different areas known as lobes (see Figure 1.6(b)): frontal, parietal, temporal, and occipital. Each lobe is in charge of the control of different specific functions: 1) frontal lobe centralizes its functions in planning and movement control; 2) parietal lobe leads somatosensory system, relating body image model with the environment model captures by the senses; 3) occipital lobe rules vision; and 4) temporal lobe is in charge of hearing, as well as learning, memory and emotions [Kandel et al., 2000].

The adult human brain consists of about 86 thousand millions neurons and around the same number of glia [Azevedo et al., 2009]. It is the most energy-demanding body organ, consuming around 20 % of the total energy used by the human body [Swaminathan, 2008]. It weights around 1.4 kilograms [Kandel et al., 2000,Parent, 1996], which coincides with approximately 2 % of full body weight, and despite of that, it owns 15 % of the cardiac blood stream, 20 % of the oxygen supply of the body, and as much as 25 % of the total glucose consumed [Clark et al., 1999]. Furthermore, recent findings [Raichle and Gusnard, 2002] have shown that the brain metabolic activity remains almost invariable over time, regardless of the mental or motor activities.

Stroke is a pathologic condition that involves loss of brain function due to this abnormality in brain's blood supply, and that could be prevented avoiding certain risk factors, mainly with changes in lifestyle [Knecht et al., 2011]. It can be produced as already commented by an ischemia (lack of blood flow) caused by blockage (thrombosis, embolism); or by a haemorrhage. The most commonly accepted definition, by the World Health Organization (WHO), states that a stroke "rapidly developed signs of focal (or global) disturbance of cerebral function lasting longer than 24 hours (unless interrupted by death), with no apparent nonvascular cause". As a result the affected area of the brain loses its function as "approximately two million brain cells die every minute during a stroke" [Gund et al., 2013], which can lead to extremely heterogeneous effects, depending on the affected area and size of the lesion [Brewer et al., 2012], such as the inability to move one or more limbs on one side of the body, inability to understand or produce speech, or lateral blindness, among others [Muir, 2009, Langhorne et al., 2009, Volpe et al., 2001, Arene and Hidler, 2009]. Although a stroke can affect the entire body, the main dysfunctions that can result are: paralysis, cognitive deficits, speech disorders, emotional difficulties, mobility difficulties in daily life and pain [Serrano, 2008]. Stroke is not an uniform disease, affecting the motor, cognitive, sensorial, and somatosensory systems [Kelly-Hayes et al., 1998, Riddoch et al., 1995]. To sum up, how and to what extent it interferes with these systems depends on many characteristics, such as the nature (haemorrhagic vs. ischemic), lesion and size (dominant side, cortical vs. subcortical, cerebral lobe) of the lesion; the condition of the patient before stroke onset; and the time post-stroke. The main factors that influence the outcome of a stroke are the "time after stroke, the lesion location, and the integrity of corticospinal tracts and cortical and subcortical connections" [Johansson, 2011].

It is a medical emergency that can cause permanent neurological damage, complications, and even death. It is the leading cause of disability in adults in Europe and the U.S., and the second cause of death worldwide [Mathers et al., 2009]. Risk factors that favour this disease are ageing, hypertension, previous episodes of stroke or transient ischemic attacks, diabetes, cholesterol, smoking, atrial fibrillation, lack of exercise and overweight [Donnan et al., 2008]. The World Health Organization (WHO) situates the world average incidence of the disease in about 200 new cases per 100,000 inhabitants [Bonita, 1992]. In Spain, cerebrovascular diseases are the second cause (the first in women) of specific mortality and it is estimated that the incidence of stroke can range between 150-350 cases per 100,000 inhabitants/year [Díaz-Guzmán et al., 2008].

Among all the possible effects of CVA, motor impairment represents the most usual effect, and consists of the limitation or complete loss of motor control functionality [Langhorne et al., 2009]. The regions that may be affected when motor impairment occurs are pre-motor, motor cortex, motor tracts, and/or the associated pathways in the the cerebrum or the cerebellum (which controls balance and coordination) [Warlow et al., 2008, Langhorne et al., 2011]. Among the most important motor impairments is gait, whose affectation leads to poor ambulatory activity [Michael et al., 2005].

Regardless of the type of accident, affectation is lateralized and usually manifested at the body side opposite to the injured brain region (as represented in Figure 1.7), although a strict relationship between brain region and function has not been described. Nonetheless, they seem to have high correlation [Ribas, 2010]. This lateralization has the major effect when leads to hemiparesis. This condition has been reported to have a prevalence higher to 80 % of acute strokes, and more than 40 % of chronic strokes [Hatem et al., 2016]. A study by Lawrence et al. quantified "the prevalence of acute impairments and disability in a multiethnic population of first-ever stroke" [Lawrence et al., 2001], reporting motor deficits of 72.4 % and 77.4 % for lower and upper extremities respectively. Motor deficits imply reduced level of movement, potentially leading to

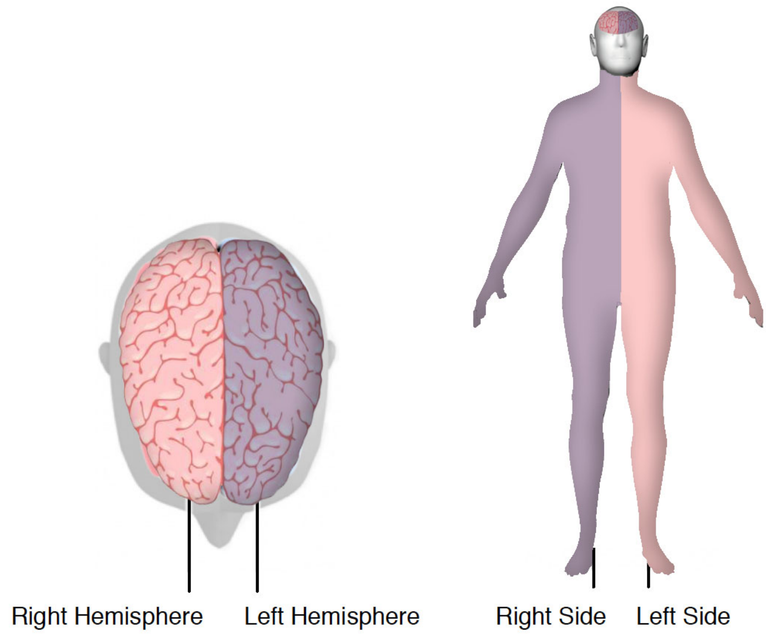


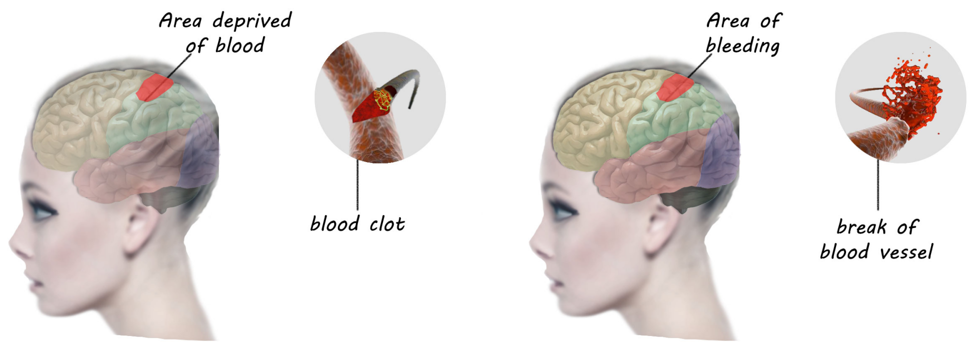
FIGURE 1.7: Functions seem to be related to regions of the human brain, and generally, there is a contralateral relationship between the brain and the body: right hemisphere is in charge of left side of the body, and viceversa.

muscle, connective and neural tissue changes [Pollock et al., 2014]. This hemiparesis effect affects also gait [Jørgensen et al., 1995, Duncan et al., 2005], and has a negative impact on both the affected and the unaffected leg on output forces and walking speed [Jørgensen et al., 1995], as they tend to avoid weight on the more affected limb [Horstman et al., 2010, Harris et al., 2001, Da Vies et al., 1996, Andrews and Bohannon, 2000].

Stroke can be classified into two main categories as mentioned before:

Ischemic stroke

Ischemic stroke is caused by the interruption of blood flow. About 80 % of cases are caused by ischemic stroke [Donnan et al., 2008, Knecht et al., 2011, Thrift et al., 2001]. In the cases of ischemic stroke, blood supply to some part of the brain diminishes or disappears as near or inner blood vessels are occluded, generating the appearance of an infarcted area, as no oxygen arrives to brain cells, which leads to a dysfunction of the tissue in that area (see Figure 1.8(a)) even if tissue's structural integrity is intact [Fisher and Garcia, 1996]. The lesion consists of two regions: core and penumbra. The core is characterized by an insufficient oxygen and nutrients supply, and thus the cells in the zone die as the stock is drained. Penumbra region still has enough blood flow aided by the surrounding untouched vessels, but this situation is unstable [Williams et al., 2013]. If the blood flow is not restored in a few hours, those cells will also die due to lack of oxygen and glucose [Donnan et al., 2008].



(a) Ischemic stoke (b) Haemorrhagic stroke

FIGURE 1.8: Types of stroke.

The most commonly accepted classification method for stroke is the Trial of Org 10172 in Acute Stroke Treatment (TOAST) [Adams Jr et al., 1993, Brainin and Heiss, 2014]:

1. large-artery atherosclerosis (occlusion, due to hardening of arteries, mainly by cholesterol, of brain vessel, or intra- or extravascular, due to a blood clot or plaque fragments formed in the brain; around 30 % of the cases),
2. cardioembolism (embolus with its source in the heart, 25 % to 35 % of the ischemic stroke cases),
3. small-artery occlusion (lacunar infarcts in other classification methods; common to chronic diabetes, hypertension and/or smoking condition; around 30 % of the cases),
4. stroke of other determined aetiology (due to other blood diseases or conditions that tend to coagulate), and
5. stroke of undetermined aetiology (or cryptogenic, one third of ischemic stroke cases [Guercini et al., 2008]).

The inconsistence on the total number of cases in relation to the individual occurrence of each type is due to the possibility of overlapping causes that lead to this kind of stroke [Brainin and Heiss, 2014].

Haemorrhagic stroke

Haemorrhagic stroke is caused by the rupture of a blood vessel or abnormal vascular structure. The occurrence of this type of stroke represents only 10 to 20 % of stroke cases [Ikram et al., 2012]. Intracranial haemorrhage is as its name indicates the accumulation of blood anywhere within the skull area, due to rupture in a blood vessel (see Figure 1.8(b)). A distinction is made between intra-axial bleeding (blood within the brain, the most common [Brainin and Heiss, 2014]) and extra-axial bleeding (blood inside the skull but outside the brain, *e.g.* provoked by amyloid angiopathy [Williams et al., 2013]). Intra-axial bleeding is brought about by intraparenchymal or intraventricular haemorrhage (blood in the ventricular system). The main types of extra-axial haemorrhage are epidural hematoma (bleeding between the dura mater and the skull), subdural hematoma (bleeding in the subdural space) and subarachnoid haemorrhage (between the arachnoid and pia mater). The extravasated blood exerts compression on the brain structures, increasing the affected area and the likelihood of a new break; and causing cell dead.

Hypertension is one of the main mechanism responsible for the haemorrhagic stroke, leading to aneurisms that usually end in vessel rupture [Auer and Sutherland, 2005], and although its occurrence is lower than that of the ischemic type, death rates are higher [Brainin and Heiss, 2014]. It has been reported that "about two-thirds of patients with primary cerebral haemorrhage have either pre-existing or newly diagnosed hypertension" [Donnan et al., 2008, Thrift et al., 1995].

1.3 Rehabilitation after stroke

In the cultures of the antiquity, disabilities were considered punishment from a religious or mythological point of view, and thus impaired people could not be treated but refused [Khasnabis et al., 2010]. But as science advanced over the last century, a more medical point of view gained ground, leading to the rehabilitative approaches. Furthermore, the policy of non-intervention that often led to high dependency states and premature death has evolved into a policy that entails as much as possible the increase in the intensity of therapy with the result of increasingly better survival expectations. The WHO [World Health Organization, 2011] defines rehabilitation as "a set of measures that assist individuals, who experience or are likely to experience disability, to achieve and maintain optimal functioning in interaction with their environments". Motor impairment originating pathologies, and stroke is not an exception, lead to dependence of the patient and compromise quality of lije on the DLAs, as pathologies are usually associated with other non-motor impairments [Langhorne et al., 2009]. Consequently, rehabilitation focuses on providing the people, to the possible extent depending on their pathology, with this lost independence, and on improving their quality of life.

The easiest solution is to provide the affected person with a caregiver, but the truth is that it does not repair the serious incidence, since it still supposes a dependence; in addition to the low self-esteem that it entails, and the loss of personal autonomy, which makes that many of them enter a spiral of negative evolution. In these situations, palliative alternatives are presented such as surgical interventions and pharmacological; and the focus of this work: physiotherapeutic rehabilitation treatments.

1.3.1 Why focus on stroke?

Disability is a complex condition, which reflects the interaction between the human being with his/her condition and the environment in which he/she lives and develops his/her life. People with disabilities are currently the world's largest "minority". According to the WHO, its number exceeds 1,000 million or, in other words, 15 % of the planet's population [World Health Organization, 2011]. The "Convention on the Rights of Persons with Disabilities" includes in this group all those who "have long-term physical, mental, intellectual or sensory impairments which in interaction with various barriers may hinder their full and effective participation in society on an equal basis with others" [United Nations, 2006]. Therefore, it is necessary to break down environmental and social barriers, as well as to adapt the means to achieve social inclusion and the full participation of these people, with the same social, labour and personal rights.

From a wider point of view, we can define the disease burden as the social impact of a specific pathology. The most widely accepted and reported factors to measure that impact in stroke are: death, incidence and prevalence rates, social cost, and the potential disabilities due to the pathology. Death rate is one of the most widely used metrics, as it has the potential to provide health managers with clues to plan the health policies. In the period from 1980 to 2017, the Global Burden of Diseases study (GBD) found that, within a group of 195 countries, the second disease with the higher death rate was stroke [Global Burden of Disease Collaborative Network, 2018] (approximately 6.2 million people, see Figure 1.9). In 2018, there were 13.7 million first-ever stroke affected people, and up to 80 million stroke survivors [World Stroke Organization, 2018b], which represents an increase of 27.20 % on first-ever stroke affected people, and, more importantly, 38.26 % increase of stroke survivors, since 1990 [Global Burden of Disease Collaborative Network, 2018], with a shift of the burden towards younger population. The GBD study also found that, in Spain, there was an increase in the incidence of 26.23 % and a prevalence of 26.36 %, with a promising death rate reduction of 40.00 % in the period between 1990 and 2017.

But all the previous factors to quantify the disease burden lack the potential to balance the given insight of the burden borne by individuals from different communities. Thus, disability adjusted life years (DALYs) lost metric was described by Murray in 1994 [Murray, 1994], stating four principles to ensure the correct balance of the measure across communities: 1) to the extent possible, any health outcome that represents a loss of welfare should be included in an indicator of health status; 2) the characteristics of the individual affected by a health outcome that should be considered in calculating the associated burden of disease should be restricted to age and sex, and nothing else; 3) treating like health outcomes, regardless of other factors, for example, the origin or the location; and 4) time is the unit of measure for the burden of disease, rather than using more location- and society-specific factors such as unit population. This DALYs lost metric is based on two components: lost years of life due to death, and years survived

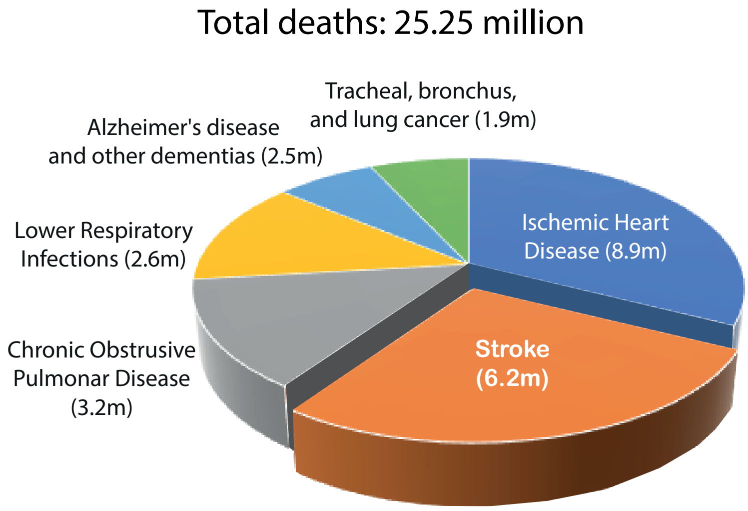


FIGURE 1.9: Burden of stroke: six most common cause of death around the world in 2017. Data available from http://ghdx.healthdata.org/gbd-results-tool.

with the disability. Similar patterns to those found on the previous metrics were found [Global Burden of Disease Collaborative Network, 2018]: 37 % increment of DALYs lost from 1990 to 2017.

According to the "Survey of Disability, Personal Autonomy and Dependent Situations (Encuesta de Discapacidad, Autonomía personal y situaciones de Dependencia - EDAD-2008)" [Instituto Nacional de Estadística, 2008] carried out by the National Institute of Statistics (INE), the number of people with disabilities in Spain was close to four million, *i.e.*, around 9 % of the population, of which 36 % could not perform the basic DLAs without help [Observatorio Estatal de la Discapacidad, 2010]. The most frequent disabilities among the Spanish population were those associated with mobility. According to the INE report, 60 % of people who declared having some type of disability also had difficulties to move out of home.

Motor impairment rehabilitation is capital as this pathology affects each year to 13.7 million people worldwide, being the second leading cause of disability [World Stroke Organization, 2018b], and thus, motor function rehabilitation is one of the cornerstones of stroke rehabilitation [Brainin and Heiss, 2014]. More than 80 % of stroke victims suffer from motor impairment [Warlow et al., 2008]. The typical cyclical process involved in the rehabilitation of motor functions guides the clinician with a logical sequence of tasks: 1) identify the patient's problems and needs, 2) relate problems to relevant modifiable and limiting factors, 3) define therapy goals, 4) planning the intervention, and 5) assess the effects of the intervention [Steiner et al., 2002]. More importantly, although there is a notable increase on the mean age of the affected people, there is still a worrying number of stroke incidence in people younger than 65 years [Feigin et al., 2014], and even more worrying, 83,000 children and teenagers (20 or younger) are affected each year.

Another very important factor to take into account, especially given the huge numbers in affectation and survival on stroke, is the economic aspect. As stated before, stroke is responsible for 10.11 % deaths worldwide [World Stroke Organization, 2018a], and supposes huge costs every year, representing 2 to 4 % of the direct health-care costs worldwide, and more than 4 % in industrialized countries [Donnan et al., 2008]. Having a survival rate of about 80 % stroke victims, it means that is the second most common cause of death, but the first of disability in the long-term [Global Burden of Disease Collaborative Network, 2018, World Health Organization, 2003], mainly, motor impairment [Wade, 1992], and more precisely, the leading impairment is in gait [Mauritz, 2002]. In Europe, the total cost per year oscillates around 64.1 thousand million € (in prices of 2010) [Olesen et al., 2012]. In Spain, these numbers are of 27,711 € per patient and year [Alvarez-Sabín et al., 2017].

These data above presented show that there are increases in all the possible factors related to the stroke disease burden: mortality has increased, and there is an increasing number of affected people; but luckily there are more survivors, and thus DALYs lost is greater too. The prognosis for year 2030 delivers numbers of almost 12 million of deaths due to stroke, 70 million of stroke survivors and more than 200 million DALYs lost [Feigin et al., 2014]. All these figures, and the reasoned fact that stroke is the principal neurological disease in the developed world that culminates in physical disability, present stroke as an optimal candidate for the focus of motor impairment rehabilitation [World Health Organization, 2011, Bonita et al., 2004]. Furthermore, the decreasing but real presence of the disease on people with much years to live, together with the improvement on the quality of life and longevity of the survivors, present a profound rationale for the focus on this disease.

1.3.2 Therapy factors

This subsection traces the different aspects for a potentially successful treatment on the rehabilitation after stroke.

1.3.2.1 Early therapy

There is evidence that promoting the earlier incorporation of stroke patients to the rehabilitation therapy, increasing the level of intensity and frequency of the exercises, and enabling the maintenance of therapeutic methods in DLAs, lead to significant improvements in the treatment outcome, [Kollen et al., 2006, O'Dell et al., 2009, Teasell and Kalra, 2005, Bogey and Hornby, 2007, Dewey et al., 2007]. The evidence seems to indicate that the improvements are mostly related to the early onset of therapy, and the intensity of it. There is spontaneous recovery of function within the first six months, larger improvements occurring within the first three, that together with the early onset of the therapy, leads to greater prospect of recovery [Jørgensen et al., 1995] and better outcomes from the rehabilitation therapy [Van Peppen et al., 2004, Katherine Salter et al., 2006, Cifu and Stewart, 1999]. However, there is evidence that states that the chronic phase can also present recovery [Teasell et al., 2005, Dobkin, 2004]. This recovery behaviour, improved in the early stages of the disease, may be explained by the fact that the ipsilateral neighbouring areas of the brain damaged region, or the corresponding contralateral region (it depends on the compromised area) sometimes assume the functions of the damaged brain region, being the sooner they make the assumption the better [Pulsifer et al., 2004]. Furthermore, there are some studies presenting strong evidence of task-oriented training assisting the "natural pattern of functional recovery" [Langhorne et al., 2011].

1.3.2.2 Therapy phases

As mentioned in the Introduction, gait rehabilitation therapy can be described by two phases [Schmidt et al., 2007, Belda-Lois et al., 2011]: T1) preparatory training based on joint mobilization; T2) gait restoration, followed by the improvement of gait in order to meet the requirements of daily mobility. In T1, the patient trains gait-oriented lower limb movements, which are performed with and without therapist intervention. The aim of this procedure is to control the evolution of spasticity and to strengthen the muscles and joints necessary for standing and walking, *i.e.*, ankle, knee, and hip. Because of spasticity is mainly related to an hyperactivity of ankle plantar-flexor muscles, we will only consider ankle movements when further referring to T1. As soon as the patient is able to maintain a standing position for 10 minutes or more, it is acceptable to proceed to T2 [Knecht et al., 2011]. In T2, the patient participates in sessions of gait training, which can be assisted by a human therapist or a robotic orthosis, or by the combination of both [Mehrholz et al., 2007]. In this phase, the patient trains motor coordination to re-learn and re-acquire a physiological gait pattern.

1.3.2.3 Motor learning

Regarding motor learning, it is necessary to mention its neurophysiological aspects, since the current learning and motor control theories are based on the physiology of the nervous system. Motor learning can be defined as "a set of processes associated with the practice or experience that entails relatively permanent changes in the capacity of response of an individual" [Shumway-Cook and Woollacott, 2007]. It produces relatively permanent (not short-term) changes in behavior, to produce an efficient response (adaptive to the environment) [Cabeza and Morales, 2012].

One important point to take into account in rehabilitative processes is that "several types of exercise programs, including muscle strengthening, physical conditioning, and task-oriented exercises have led to an improvement in balance and mobility" [Leroux et al., 2006]. Thus, it makes sense to focus the approach of early rehabilitation and motor recovery on simple tasks, towards the integration of them into more complex processes while the recovery takes place over time, and furthermore taking into account that motor and function impairments seem to present a direct relationship: for example, gait function is correlated to lower-limb strength (impairment) [Jørgensen et al., 1995, Langhorne et al., 2009]. Patton et al. [Patton et al., 2006] also found evidence on stroke survivors retaining ability to adapt to force fields, being better at adapting to real scenarios less demanding than training scenarios (lower forces in the real world than in the training); and more importantly, they can last longer if the exercise resembles normal movements and the after-effects can be perceived by the patient as an improvement [Patton and Mussa-Ivaldi, 2004].

Most studies are focused on upper-limb rehabilitation, but Duncan et al. [Duncan et al., 1994] demonstrated that similar motor recovery of upper and lower-limbs occur after stroke.

1.3.2.4 Neuroplasticity

Santiago Ramón y Cajal, considered the father of modern Neuroscience, stated that "once development is complete, the sources of growth and regeneration of axons and dendrites are irretrievably lost. In the adult brain the nerve paths are fixed and immutable: everything can die, nothing can be regenerated" [Ramon y Cajal, 1928], but it has been demonstrated that a fully grown CNS of an adult can present reorganization and recovery [Dimyan and Cohen, 2011, Nudo et al., 1996]. These findings suggest that undamaged motor cortex might play an important role in motor recovery, and it is important to note that motor recovery after brain injury is a form of motor learning [Krakauer, 2015] and functional recovery, mainly by optimizing sensorimotor performance in functional actions. The way the CNS maximizes rehabilitation therapies' outcome is via the mechanism of brain plasticity. Neural plasticity was described at a cellular level on the synapses by Hebb [Hebb, 1949], and has been later extended to the brain and other neural networks [Brainin and Heiss, 2014]. Brain plasticity is the mechanism that permits, via changes in synaptic connections strength [Murphy and Corbett, 2009], the adaptation to environmental challenges and experiences such as brain lesions [Nithianantharajah and Hannan, 2006, Pascual-Leone et al., 2005, Johansson, 2004]. Neurophysiology is related to motor learning in this sense (see Fig. 1.10): physiological activity is behind learning processes because the changes in the excitability of neurons may lead to plasticity in the nervous system; and motor learning leads to improvement of functional skills, so there is a need to optimally use it in our design of therapies [Aqueveque et al., 2017]. The plasticity of the brain can gain functional recovery by two different possible mechanisms, *i.e.* restitution or compensation [Dobkin and Carmichael, 2005]. In motor restitution, the function is restored in a way that the same muscle groups as before the stroke,

Figure 1.10: Relationship between motor learning and neuroplasticity.

unmasking inactive synapses or generating new ones [Rossini and Forno, 2004], leading to the same movement performance [Levin et al., 2009]; whereas in the case of motor compensation, different neural tissue assumes the function of the damaged one, using alternative muscles and compensatory strategies [Krakauer, 2006].

The recovery that takes place at a neurological level after stroke follows, starting a few hours after the stroke, a quasi-logarithmic shape (see Figure 1.11); and Langhorne et al. stated that recovery "probably occurs through a combination of spontaneous and learning-dependent processes" [Langhorne et al., 2011]. Around 6 months after the CVA, recovery curve seems to reach a plateau, that has been hypothesized to probably respond to "asymptotic learning after massed practice rather than a true biological limit" [Krakauer, 2005,Krakauer, 2006]; there are studies that show evidence of effective results after that theoretical plateau, shedding light on the possibility of neural reorganization taking place in the subacute and chronic phases [Langhorne et al., 2009, Krakauer, 2006, Hatem et al., 2016].

The underlying mechanisms behind the process of neuroplasticity are still not well understood, but can be described by these factors [Dobkin, 2004]: 1) evolution of neuronal representation for skilled movements, formerly of latent synapses; and recruitment of areas correctly working before the lesion, needed when the task difficulty was higher; 2) greater excitability of the neurons and higher synaptic connection efficacy "within related

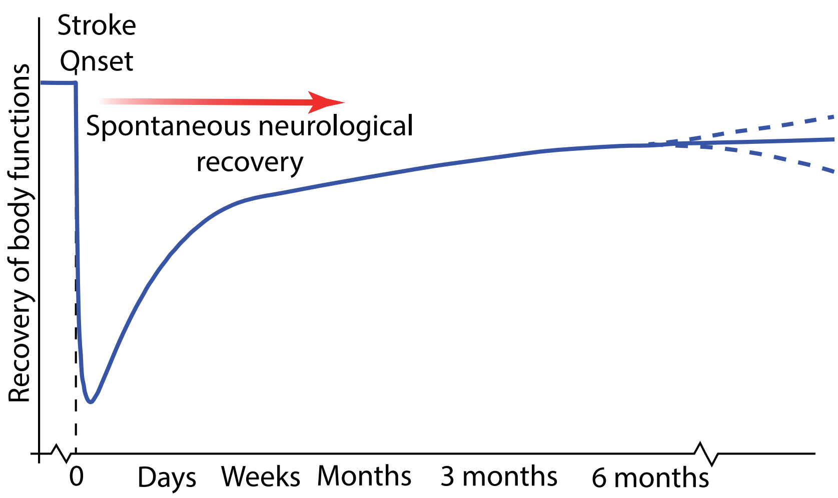


Figure 1.11: Recovery pattern after stroke: a few hours after the lesion, the recovery pattern presents a quasi-logarithmic curve, with an apparent plateau. Figure adapted from [Langhorne et al., 2011].

primary and secondary sensorimotor cortices and spinal motor pools"; 3) morphological changes in dendritic branches and spines associated with long-term potentiation (LTP) and long-term depression (LTD) phenomenons; and 4) adaptation of still functioning cortical, subcortical, and spinal networks for skilled movement. It is capital for a successful treatment to take into account that adaptive plasticity not always leads to a functional recovery, leading in many cases to maladaptive plasticity [Dimyan and Cohen, 2011, Buma et al., 2013], so well-adaptive reorganization considers that plasticity related to motor learning leads to recovery [Krakauer, 2005].

In humans these changes in the nervous activity can be non-invasively measured via several methods, such as Hoffman reflex (H-reflex), F-wave, tendon jerk, Volitional-wave, cervicomedullary motor evoked potential (CMEP), and motor evoked potential (MEP) [McNeil et al., 2013, Richards et al., 2008, Nair et al., 2007, Stinear et al., 2006]. These techniques provide information about the state of the neurons, and also if the possible changes are durable in time.

To elicit MEP generation, we have used transcranial magnetic stimulation (TMS) technique, and thus, the next lines present a wider explanation with special focus on the muscles relevant on this work. This technique has already been used in the literature to assess the tibialis anterior (TA) excitability before and after lower limb trainings: motor imagery + electrical stimulation [Mrachacz-Kersting et al., 2012] (neuroprosthetics), or motor imagery + robot-assisted dorsi-plantarflexion [Xu et al., 2014] (neurorobotics). TMS is the technique that allows the assessment of the corticospinal excitability in a non-invasive way [Ziemann, 2017]. The TA dorsiflexor muscle is fundamental in the swing and heel strike phases of the gait, and leads to foot-drop issue when its function is compromised [Ruiz-Muñoz and Cuesta-Vargas, 2014]. Furthermore, corticospinal projection to TA motoneurons is comparable to that at upper-limb level, much stronger than to the rest of leg muscles [Perez et al., 2004]. MEP measurement via TMS is a neurophysiological measurement that allows us to check the variation on the corticospinal excitability of the target muscle, and thus provides a neurophysiological insight to be confronted to the results given by the performance values given by the robotic device and kinematic sensors' data. This focus improves the results encountered in works like Goodman et al.'s [Goodman et al., 2014] where they analyze electroencefalography (EEG) spontaneous activity during task, instead of using MEPs for the assessment of the excitability changes before and after the training. The information given by the changes observed after applying this assessment technique may be related to the TA motor control, as a decrease in the errors after a dorsi-plantarflexion movement task was encountered where increased MEPs were found [Perez et al., 2004].

1.3.3 Traditional therapy approach

Neurological gait rehabilitation for stroke can be divided in two main groups: neurophysiological techniques and motor learning.

- Neurophysiological techniques

  These techniques mainly consider the patient as a passive agent, and is the physiotherapist who performs the correct actions and solves the problems. These are the most common in gait rehabilitation after stroke [Belda-Lois et al., 2011]:

  – Bobath [Bobath and Bobath, 1957,Bobath, 1990], as the maximum exponent of "neuro-developmental treatment" (NDT) [Lennon and Ashburn, 2000,Riddoch et al., 1995, Davidson and Waters, 2000, Lennon, 2003, Beeston and Simons, 1996]. NDT focuses on the full person and not only on his/her sensory-motor deficits, taking into account development problems, cognitive impairments, emotional, social and functional problems [Veličković and Perat, 2005]. The hypothesis behind Bobath technique is that there is a relationship between increased muscle tone (spasticity) and antagonistic muscle weakness. The approach intends to perform passive movements associated with proprioceptive stimuli. It is widely accepted as a stroke rehabilitation oriented technique, but still lacks of evidence on its efficacy [Van Peppen et al., 2004,Kollen et al., 2009, Lennon et al., 2006, Hafsteinsdóttir et al., 2005, Brunham and Snow, 1992,Hesse et al., 1995,Partridge and Edwards, 1996].
  – Brunnströn method is less common than Bobath, and contrary to the former, tries to enhance pathologic synergies and uses reflex facilitation and sensory stimulation.
  – Vojta method is aimed mainly to cerebral palsy. The approach contemplates the practice of stimulating the nerve endings associated with specific physiological movement patters, to promote the activation of CPGs. The idea behind its application to stroke patients lies in the fact that the lesion does not affect the PNS nor the CNS below the brain level.

- Motor learning

  Motor learning techniques are aimed to promote gait rehabilitation with a different approach to that of the previous group: active participation of the patient is the key, and thus, it is capital for the success of the therapy that the patient understands the exercise and the potential outcome, to keep the engagement and the attention, thus enhancing motivation [Cano-de-la-Cuerda et al., 2015]. Furthermore, if the patient lacks the capacity to understand how an exercise is executed correctly, little effect can be expected [Asín-Prieto et al., 2014a]. It is important to note that stroke patients' learning function may be compromised as their brain has suffered an injury. The techniques that conform this group apply context and task-specific training, preferably in the patient's own environment [Belda-Lois et al., 2011]:

- Perfetti method, focused initially on controlling spasticity, starts with tactile recognition of different stimuli, and passes from passive to active manipulation. The idea is to deliver similar sensory input to that received while real walking.
- Motor relearning method considers that stroke survivors and healthy individuals learn similarly, that posture and movement are related, and that the task-specific motor response can be modulated via the appropriate sensory input. The active participation of the patient starts at the very beginning of the treatment, where the therapist guides the movement, so that there is lack of forced sensory input (in contrast to Perfetti method).

Although these techniques have been used for long now, their results on gait recovery have been moderate, and furthermore, non dependent on the specific technique [Krakauer, 2006]. Given the high variability of stroke patients, it was not surprising that a recent large Cochrane review demonstrated that no rehabilitation therapy was superior, with the exception of constraint-induced movement therapy for the upper limbs [Boddice et al., 2010]. Furthermore, various rehabilitation procedures with disparate underlying neurophysiological assumptions are routinely applied in clinical settings, despite being based on little or no evidence of efficacy [Belda-Lois et al., 2011]. In the past decade, several technology-based approaches to stroke rehabilitation have been proposed [Ifejika-Jones and Barrett, 2011], but evidence of their efficacy is scarce [Mehrholz et al., 2007, Morone et al., 2012].

The principle of "who wants to walk, has to walk" [Hesse and Werner, 2009] states the need for task-specific repetitions for a successful therapy. In all the previous techniques for gait rehabilitation, we have this common denominator of task-specific repetitions, and as much repetitions as possible, as to be the principle that seems to have better outcomes [Knecht et al., 2011]. A clear example of therapy, which has provided good results regarding task repeatability and task focus, is over-treadmill gait training, with a harness to unload and support patient's weight [Hesse et al., 1995, Lau and Mak, 2011, Franceschini et al., 2009, Laufer et al., 2001, Macko et al., 2005, Pohl et al., 2002]. In traditional therapy, physical therapists assist manually the legs movements (so at least two are needed, one for each leg, and this -more than one therapist per patient- is something health systems do not always cover), providing guidance in an assist-as-needed (AAN) manner, *i.e.* as much assistance as the patient needs to perform the task. But this approach has the problem of being an intensive exercise not only for the patient, but also for the therapists, leading to potential work injuries and diminishing the possible repeatability.

Technology has provided a great solution to this important limitation, as robots (from the Czech word *robota*, literally corvée, or slave hard worker [Čapek, 1920]) are great at repeating without the problem of extenuation or physical lesions on physiotherapists, being a remarkable tool to assist them on physiotherapy programs targeting neurological impairment [Jezernik et al., 2003]. They provide also another feature along with the repeatability: they provide objective measurements of joint kinematics and kinetics [Volpe et al., 2001, Hidler et al., 2005]. Next subsection briefly extends the current status of the robotic field motor rehabilitation-wise, provides some of their advantages and lacks and synergistic combinations with other technologies, and very briefly presents some existing systems that motivate this work.

1.3.4 Robot-aided therapies

We are witnessing an exciting era in which robotic technology for the rehabilitation of motor disorders is being introduced into clinical use, and are, from a technological point of view, the most studied gait rehabilitation tool [Jezernik et al., 2003, Peurala et al., 2009, Veneman et al., 2007, Freivogel et al., 2008, Patton et al., 2008, Stauffer et al., 2009, Kwa et al., 2009, Saito et al., 2005, Costa and Caldwell, 2006, Sawicki and Ferris, 2009, Moreno et al., 2008, Blaya and Herr, 2004, Krebs and Hogan, 2006, Wheeler et al., 2004, Bortole and Pons, 2013, Asín-Prieto et al., 2012]. Advances in computing, materials, sensors, interfaces and manufacturing processes, along with the incorporation of basic knowledge of the neuro-physiological principles involved in motor recovery into *intelligent* controllers, are enabling better rehabilitation services. Indeed, as a comparison, where a manually assisted therapy of typically 30 minutes can reach up to 100 steps per session, a robot assisted therapy can let the patient reach a training of around 1,000 steps in the same amount of time [Schmidt et al., 2007, Huang and Krakauer, 2009]; and it has been concluded that its efficacy is at least the same as that of the conventional therapy, requiring less effort from the clinicians [Werner et al., 2002, Huang et al., 2017], and potentially raising the cost-effectiveness ratio of the rehabilitative therapy [Reinkensmeyer et al., 2012]. It is worth pointing again that this need of intensive repetition, although potentially promoting neuroplastic mechanisms to improve gait function [Dietz, 2008, Dietz, 2003, Curt et al., 2008], they may lead to health problems for physiotherapists, and robotics can be of huge help in providing them with a tool to enhance the therapy by allowing them to ensure repeatability, as they help the physiotherapist to provide an objectively equal movement to the patients limb, and providing a tool to more objectively assess performance metrics [Patton and Mussa-Ivaldi, 2004]. The principle of motor recovery through intensive repetition relies on motor learning mechanisms, but also relies on user's motivation [Krakauer, 2006, Huang and Krakauer, 2009]. Objective assessment takes advantage of the sensors embedded in the robots, and provides information to the extent of those sensors, *i.e.* kinematics and dynamics. They can be used for the assessment of the motor impairment in specific moments and for the evolution of the pathology, providing relevant metrics for the customization of the rehabilitative treatment [Huang and Krakauer, 2009].

Many therapists focus primarily on the motor aspect of post-stroke rehabilitation, but the influence of cognition and mental state on the potential of motor recovery cannot be ignored. Motivation and attention are considered key elements in the success of motor recovery [Cramer et al., 2011]. A patient needs to understand why a certain exercise is proposed: specific exercises need to make sense, and goals must be clear to enhance motivation. If one lacks the capacity to understand how an exercise is executed correctly, little effect can be expected. Furthermore, if one is depressed and unable to see the value in recovery of motor function, focusing on such a goal might not be the most appropriate at that time.

Considering the entire interaction of the motor recovery-cognition-mental state system in a patient, it is often claimed that therapeutic interventions should be functional. To ensure adherence and maximum effort by the patient towards rehabilitation, therapeutic exercises should focus on walking or picking up a glass instead of knee flexion and elbow extension. Consistent with this approach, the Institute of Medicine (IOM) defines patient-centred care as "health care that establishes a partnership among practitioners, patients, and their families (when appropriate) to ensure that decisions respect patients' wants, needs, and preferences and that patients have the education and support they need to make decisions and participate in their own care" [Baker, 2001]. An important element of this definition is the "establishment of a partnership" between the patient and caregivers to meet the needs of the former. This partnership comprises more than one individual, and all participants' needs should be met for it to be successful and for optimal therapeutic profit to be gained. It is also an important aspect that increases the variability between rehabilitation approaches is the interaction between the patient and his/her therapist. An empathic therapeutic relationship might support or interfere with the treatment, the mental state of the patient during rehabilitation, one's tendency to collaborate, and the general psychological reaction to the stroke [Scott et al., 2012].

1.3.4.1 Exoskeletons

In the beginning of their spread, robots were built for industrial environments with the aim of alleviating manpower, but they have been proven over the years to be a useful tool in a wider group of tasks. Amongst these devices, robotic exoskeletons for gait rehabilitation are currently the subject of functional, basic (*i.e.*, neurophysiological) and clinical research thanks to the availability of marketable, thus safe and robust, devices, which allows prolonged experimentation to gather data regarding efficacy and clinical outcomes [Pons, 2008]. These devices can be passive (provide weight support and gravity compensation, or imposed motion: "robot-in-charge") or active ("patient-in-charge", the robot reacts when the patient moves, see Figure 1.12) [Meng et al., 2015].

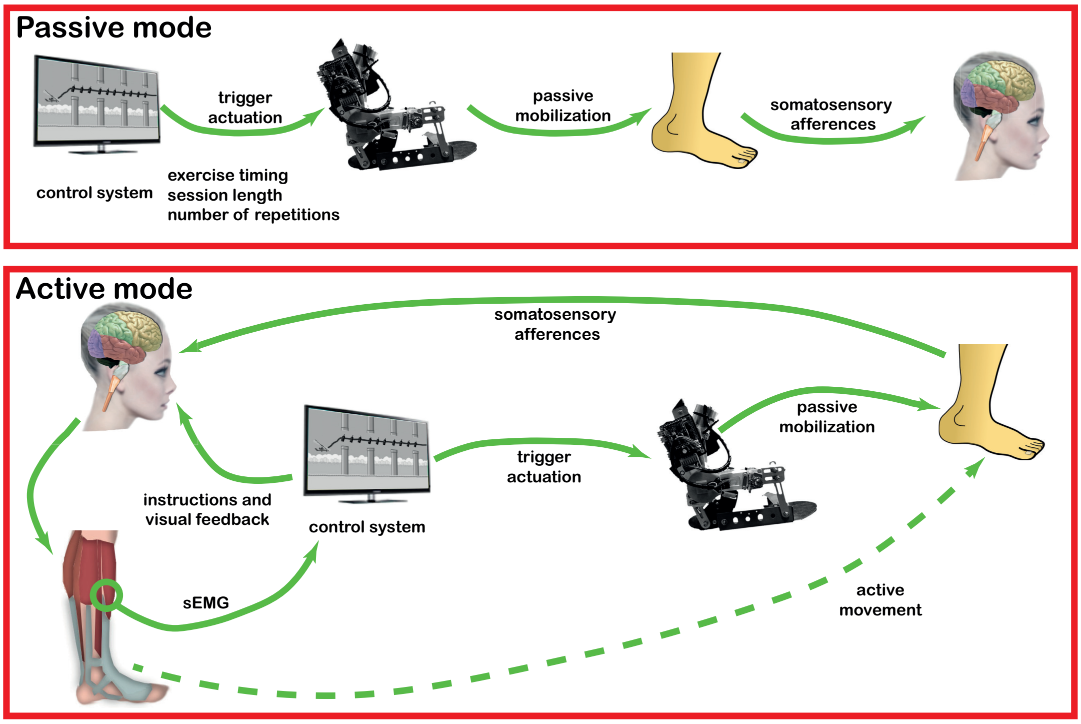


FIGURE 1.12: Passive mode and active mode. sEMG stands for surface electromyography.

The latter group can be assistive (providing guidance to the movement, with a huge range of possibilities, from low assistance to full guidance), resistive (resisting the user movements to demand more effort on the task) or a combination of both, depending on the phases of the task or training. Robotic exoskeletons can also be divided into assistive and rehabilitation devices, from a more wide point if view, where the former is aimed to remain in the group of aiding devices such as canes, crutches, walkers or wheelchairs; whereas the latter, of more interest within this work and main focus of it, provides a valuable tool for gait (and other motor tasks and functions) recovery [Krebs et al., 2008]. Nonetheless, the effectiveness of locomotor therapy is limited regardless of the training approach [Nooijen et al., 2009, Morawietz and Moffat, 2013, Wessels et al., 2010, Swinnen et al., 2010, Mehrholz et al., 2017, Dobkin and Duncan, 2012], and it reveals that these technologies still present lacks that make them not clearly superior to the traditional therapy. One possible origin for this limited outcome may lie in the fact that if the therapy device is too complex, the learning required from the clinicians is higher, and the application gets more difficult at the clinical setting [Riener et al., 2005]: thus simpler (less degrees of freedom -DoFs-) and task-specific devices could better exploit the benefits of this technology for rehabilitation, and this is the reason why we focused in this work in the ankle joint for dorsi-plantarflexion (1 DoF, specific task).

1.3.4.2 Which approach is better? Traditional vs. robot-aided therapies

There have been a number of studies seeking to demonstrate the efficacy of robotic-based therapies and their superiority over traditional approaches, but the literature is non-conclusive, as there are some publications yielding more favourable results for robotic-aided therapy alone [Werner et al., 2002, Mayr et al., 2007, Schwartz et al., 2009, Tong et al., 2006, Pohl et al., 2007], some conclude that robotic-aided therapy is empowered while combined with conventional approaches [Peurala et al., 2005, Husemann et al., 2007, Westlake and Patten, 2009], and there are even some that provide evidence yielding the superiority of conventional therapy [Hidler et al., 2009, Hornby et al., 2008]. This controversy mainly depends on the inclusion/exclusion criteria and on the chosen outcome measures. For these reasons, Morone et al. proposed to change the question "Is robotic-assisted training effective?" into "Who may benefit from robotic training?" [Morone et al., 2011]. When evaluating new methods, one should focus on patient-related disabilities and the expectations and goals of the patient and his/her caregivers for rehabilitation (International Classification of Functioning, Disability and health [World Health Organization and others, 2001]).

In comparison with traditional gait training, robot-assisted movement repetitions are more homogeneous, and the number of repetitions and training intensity can be increased. A recent review analyzing seventeen clinical trials (837 participants) reported that robotic gait training, in combination with conventional physiotherapy, increased the probability of recovering walking independence in respect with conventional therapy alone, but did not increase the walking capacity or speed [Mehrholz et al., 2017]. The best outcome for rehabilitation after stroke seems to come from the combination of both traditional and robotic-aided approaches in the therapy, as a recent Cochrane review on 23 trials exposes [Mehrholz et al., 2013]; and there is also evidence of the superiority of the approach in individual factors: improved mobility [Hesse et al., 1995, Westlake and Patten, 2009], functional gait gaining [Werner et al., 2002, Hesse et al., 2001], more physiological muscle activation [Mayr et al., 2007, Hesse et al., 2001], increase in gait speed [Mayr et al., 2007,Nikamp-Simons et al., 2009] and improved joint range of motion [Nikamp-Simons et al., 2009].

1.3.4.3 Neurophysiological implications

Recent approaches claim that robot-assisted walking arises from the interaction between the human body, driven by the central nervous system through the muscles, neural loops, reflex mechanisms, etc., and the mechanical structure, driven by the controller through the joint actuators and sensors [Moreno et al., 2014]. However, there are few articles that address the interplay between the neural and robotic structures. The literature suggests that the CNS tries to reduce muscle activation when an external joint torque is provided, maintaining a total joint torque (human + robot) that resembles the natural torque profile [Lewis and Ferris, 2011, Galle et al., 2017, Zhang et al., 2017, Cajigas et al., 2017] without altering the basic mechanisms of muscle coordination [Moreno et al., 2013]. In contrast, some studies have shown that robotic assistance can result in increased muscle activation [Lenzi et al., 2013, Sylos-Labini et al., 2014], altering joint kinematics [Knaepen et al., 2014,Lenzi et al., 2013], even while walking in zero impedance mode [Van Asseldonk et al., 2008]. This problematic regarding the lack of consensus on wether the effects on the muscle activation while using a robotic device is higher or lower probably depends on the capacity of the device to adapt to the environment, thus being able to provide more or less assistance/resistance as a function of the measured interaction. Deeper into the problem, when these rehabilitative approaches are used, it is still unclear which the better way to assess the contribution of the robot and the wearer to the final task is.

In general, these machines are in intense physical and cognitive interaction with the user, and are intended to compensate the mechanics to perform a wide range of locomotor tasks. Thus, available WRs can provide control as a function of the residual signals from affected muscles [Kawamoto et al., 2003, ReWalk, 2018, Ferris et al., 2005, Blaya and Herr, 2004], apply fixed compensations as a function of gait events [Moreno et al., 2006,Saito et al., 2005], be manually controlled by the user [Rex Bionics, 2018], combine manual control and detection of gait events [EksoGT, 2018], minimize the interaction between the user and the robot [Kwa et al., 2009, Pratt et al., 2004, ihmcROBOTICS, 2018]. In these devices, transparency and easiness of use are still an issue that must be addressed. Gait rehabilitation consists ideally in providing torque to the affected joint. This implies delivering an adaptable amount of torque depending on the movement deficit, in order to allow the patient to improve the residual control. This concept originated the aforementioned AAN therapy paradigm ([Hogan, 1985]). In the AAN approach, the delivery of torque is hypothesized to be better provided under the challenge point theory ([Guadagnoli and Lee, 2004]), which claims that rehabilitation outcomes are maximized when an adequate effort is demanded from the patient without being excessive (see Figure 1.13): the patient alters the natural operation of the central nervous system, whose effects can vary from weakened muscle contraction to excessive contraction (spasticity).

1.3.4.4 The role of intensity and perseverance

Although one key factor in a successful therapy for motor recovery is the concept of repetition, the mere idea of just repeating a fixed movement is insufficient [Krakauer, 2006, Reinkensmeyer et al., 2012], and the addition of randomness in either the assistive or resistive treatment enhances the outcomes of the therapy, as the idea of “repetition without repeating” is important for the avoidance of disengagement during the progress of the task, and it emphasizes the challenge-point-theory approach. This concept of “repetition without repeating” considers that training sessions must include recording the

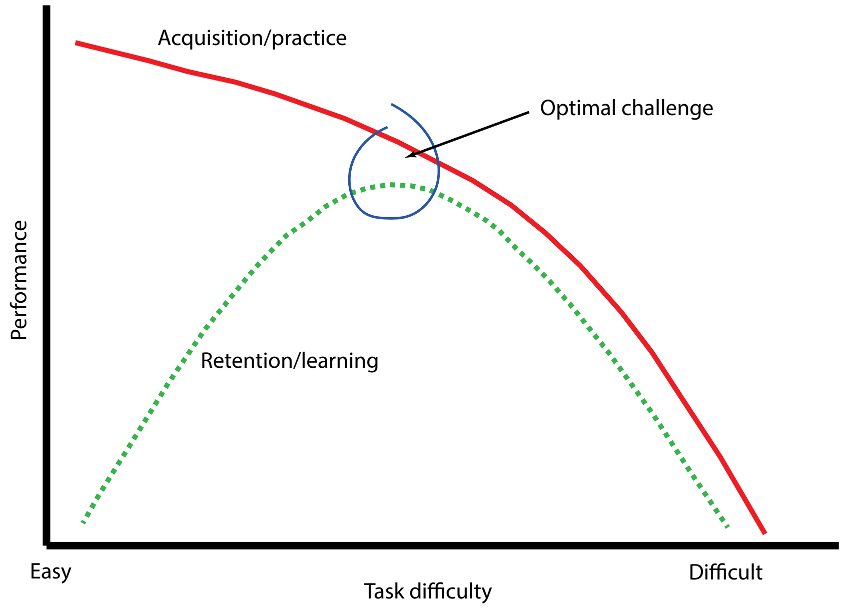


FIGURE 1.13: Challenge point theory: solid line represents the relation between task difficulty and the performance. Dotted line represents a similar concept but including learning. Then, solid line shows the decrease of performance with the increase of the difficulty, whereas the dotted line shows that in the beginning, the performance is low for easy tasks, this performance increases with difficulty due to learning, until the optimal challenge point is reached, where the challenge is the best to promote learning. Over that point, the task difficulty is too high, and thus performance is reduced.

modified parameters to challenge the patient [Cano-de-la-Cuerda et al., 2015]. Within this concept, the idea of interleaving different exercises also arises, and it has been seen that this mixing of learning tasks is more effective for learning than learning the tasks one by one with specific focused trainings [Shea and Morgan, 1979], and this mixed schedule might aid recovery because it considers each movement as a problem to solve and not as a pre-memorized muscular sequence [Krakauer, 2006].

In fact, Shea and Kohl [Shea and Kohl, 1991] stated that "retention of the test task was best facilitated by acquisition practice that included task variations rather than conditions that included additional practice on the test task or even a condition identical to the retention condition." The nervous system seems to rely on the concept of adaptation, meaning that a previously learned skill can be recovered after a change in the operating environment. This theory of adaptation says that after a change in the environment dynamics, the control system does not need to relearn but adapt, suggesting that the nervous system tunes a learned internal model and has the ability to extrapolate this learning to new scenarios [Conditt et al., 1997].

1.3.4.5 Control approaches

The implementation of different control algorithms make possible to modify the behaviour of the robotic device during the treatment [Marchal-Crespo and Reinkensmeyer, 2009]. Thus, this algorithm customization provides the feature of treatment personalization to fit user-machine interaction, but the right implementation is critical to promote learning [Reinkensmeyer and Boninger, 2012, Huang and Krakauer, 2009, Harwin et al., 2006]. Several authors have tested the error augmentation approach [Patton and Mussa-Ivaldi, 2004, Emken and Reinkensmeyer, 2005, Patton et al., 2006, Scheidt et al., 2001] to enhance motor learning. In the error augmentation approach, the movement error by the patient is increased by the perturbations, so the compensatory strategies tend to reduce this error. The nervous system learns forming the internal model of the dynamics of the environment via a process of error reduction. Emken and Reikensmeyer concluded that motor learning process can be accelerated by exploiting the error-based learning mechanism. They used the approach of perturbing the movement via a robotic device, to augment the error while the user was performing the task. It seems that this learning process is indeed a minimization problem, based on the last performed trials to accomplish the task [Scheidt et al., 2001], where the minimization takes place between the weighted sum of the kinematic error and the muscular effort [Emken et al., 2007]. Moreover, this error augmentation strategy produces, when the after-effects are evaluated, the correct muscle activation patterns to achieve the desired trajectory, and results showed that subjects were able to reduce errors more rapidly than those that received a robotic guidance approach training [Reinkensmeyer and Patton, 2009]. Reikensmeyer and Patton suggest combining robotic guidance and error augmentation techniques, starting with guidance and gradually removing it and increasing error augmentation. Indeed, this increased difficulty paradigm may be related to plastic changes at the cortical level and thus to a motor learning mechanism [Perez et al., 2004]. Marchal-Crespo et al. [Marchal-Crespo et al., 2014] showed that random disturbances improved motor learning in the performance of a simple dorsi-plantarflexion task, because this variability may increase recovery by increasing the needed effort and attention into the task. Thus they performed a new study [Marchal-Crespo et al., 2017] showing that "challenge-based" controllers, where guidance was given on the first stages of the recovery, and error augmentation on the next and last stages of the rehabilitation, were more beneficial for the recovery, as the therapy adapted to the patients. In this error augmentation phase in the study, increasing errors lead to beneficial after-effects on gait, as it rendered the exercise more difficult to be performed: for example, amplifying gait asymmetries lead to adaptation to a more symmetric pattern. This adds intensity to the training and probably serves as a stronger learning stimulus pushing them out of the "comfort zone" and encouraging investigation on the new motor tasks. But it is important not to provide too high perturbations to the movement so they can be discouraging [Turner et al., 2013]. Wu et al. [Wu et al., 2014] also showed that high levels of task-relevant variability lead to facilitated motor learning. Combined haptic error augmentation and visual feedback have provided better results than conventional direct training (pure joint mobilization), exploiting the idea of using the after-effects of a resistive force to help perform the user the desired trajectory task [Bittmann and Patton, 2017].

1.3.4.6 Robotic therapy in stroke

Robotics have been proposed and partially proven to be beneficial in interventions in acute and chronic stroke patients [Fasoli et al., 2003, Volpe et al., 2000, Krebs et al., 1998]. Several studies have been conducted with stroke patients, showing promising results comparable to those learning results seen in healthy subjects. It is important to study the better trade-off between the learning rate and the amount of helping guidance given by the robot during training [Reinkensmeyer and Patton, 2009]. Robotic guidance approaches also offer a powerful tool in rehabilitative and learning cases where large errors may be dangerous or undesirable, as this guidance provides the user with a tunnel inside of which the movement is allowed and controlled outside of it [Ren et al., 2011]. However, robotic guidance may improve success rates in accomplishing tasks in acute phases of the pathology thus motivating the subject, and this might promote learning via Hebbian-like plasticity mechanisms by increasing the amount of proprioceptive inputs, but might as well reduce patient effort and thus reduce the benefit of the therapy [Rowe et al., 2017]. For example, Patton et al. [Patton et al., 2001] found some preliminary evidence that showed that the approach of error augmentation could be used to obtain smoother trajectories in stroke patients, and this smoothness parameter has been used by Goodman et al. [Goodman et al., 2014] to provide an insight of the performance on the trajectory following task. Krakauer [Krakauer, 2006] found that, although guidance approach leads to better performance during the training, it is not optimal for retaining the learning over time, so these training may improve performance in the clinical environment, but may not be transferable to DLAs. Reikensmeyer and Patton demonstrated that with this error augmentation approach, stroke patients can potentially alter abnormal limb movement patterns that appear relatively fixed, although the reasons why people with stroke perform abnormal patterns remain to be identified [Reinkensmeyer and Patton, 2009].

Besides motor impairment, stroke patients often present somatosensory disturbances that reduce the perception of body movements. Extrinsic biofeedback compensates the affected proprioception by providing information about the motor task and performance during motor rehabilitation. There is evidence suggesting that biofeedback enhances motor learning [Van Vliet and Wulf, 2006] and improves the functionality of lower limbs after stroke [Stanton et al., 2011]. Moreover, vision plays an important role in posture control during standing and walking [Logan et al., 2010]. Hence, it is assumed that visual feedback during gait training could impact motor learning and functional recovery. Additionally, realistic dynamic virtual environment can be used to increase patient's engagement and participation, and thus adherence to the therapy [Krakauer, 2006, Merians et al., 2006]. Similarly, it has been suggested that the efficacy of a robotic-training may heavily depend on the capacity of the rehabilitation team to most effectively tailor the robotic therapy to each patient's needs [Iosa et al., 2011]. Nevertheless, a main concern is that robotic assistance may negatively influence the patient's active participation because the robot is able to complete the movement without patient's intervention [Hidler et al., 2005, Israel et al., 2006]. Since active movement contribution is necessary for encoding motor memory [Lotze et al., 2003], controlling engagement and active participation is crucial.

1.3.4.7 Improved visual feedback approaches: serious video games

In the line of providing enhanced feedback to the patients to promote motivation and engagement of the patient to the treatment, robotics can be used in combination with visual feedback interfaces, providing the possibility of showing both the patient and the physiotherapist the feedback of the performance of the task, which has been proven to improve rehabilitation [Asín-Prieto et al., 2014a]. In the literature we can find that visual feedback through virtual environments helps to improve the performance in specific tasks, even improving the results in comparison to real-task training [Todorov et al., 1997]. Indeed, this visual approach has been proven to improve robotic haptic guidance therapy scenarios [Liu et al., 2006]. Furthermore, the idea of this virtual environment or video game makes the implicit learning process transparent for the user, not being aware of what is being learned [Patton and Mussa-Ivaldi, 2004]. They also ease to offer the user with a goal-oriented task and possibility of repetition [Dobkin, 2004].

Video games seem to be effective for improving function and health after stroke, and enhance motivation [Swanson and Whittinghill, 2015]. It is important though to take into account that this video game must be simple enough not to discourage the player, *i.e.* the patient; that the game environment is better when explicitly designed for the therapy than when trying to apply commercially available games; and furthermore, that commercial games are unable to record all the useful measurements that may be needed for the therapist to check the improvements [Marston and Smith, 2012]. The use of this kind of approach with only a goniometer has been proven efficient in improving motor control from the point of view of error reduction in the trajectory performing for healthy subjects [Perez et al., 2004]. In the literature, we also find that Goodman et al. [Goodman et al., 2014] used Anklebot robotic device to control, via dorsi-plantarflexion, a video game where the level of assistance of the robot was decreased when performance increased and viceversa, and assessed this performance with the smoothness in the execution of the trajectories. And we can also find studies such as that by Ren et al. [Ren et al., 2011], where they also used a motorized ankle foot orthosis, introducing resistance in the control to rise the level of difficulty while they lowered the level of assistance when the performance of the subject was rising.

1.3.4.8 Summary

Summing up, the upcoming challenge for researchers and clinicians will be to implement one optimal rehabilitation therapy to the right patient at the right time, because certain stroke patients are better responders to a specific therapy than others, solutions must be adapted to each patient. An interdisciplinary step-by-step approach begins with increasing our understanding of physiopathological mechanisms after stroke to favour training-induced plasticity by developing tools that promote functional recovery. Despite the efforts that are being made to develop rehabilitation techniques, there are no accurate guidelines or prescriptions to guide the optimal solution for each patient. One emerging concept likely relies on incorporating objective measurements into the clinical diagnosis before and during treatment to mold the therapy to a patient's individual needs [Backus et al., 2010].

1.3.5 Current state-of-the-art devices that motivate this thesis

Based on recent reviews [Zhang et al., 2013, Basaha et al., 2017], the following lines describe some devices used in studies for stroke that motivate the work on this thesis:

- **Rutgers ankle**

  Several studies use this device, with a similar therapy approach. The authors present the use of Rutgers ankle, a quite complex to control ankle rehabilitation robot with 6 DoF, for a rehabilitation therapy with video game-based feedback [Boian et al., 2002, Deutsch et al., 2001, Deutsch et al., 2004]. It uses an haptic controller, providing resistance according to randomly positioned on-screen items. The video game difficulty is fixed at the beginning of the training, and it can be adjusted via the virtual environment parameters (weather, visibility).

  Mirelman et al. performed a study comparing the use Rutgers ankle with and without the above described virtual environment [Mirelman et al., 2009], and found significant better outcome in the video game coupled treatment.

  In another study with this device [Deutsch et al., 2007], they propose a similar approach, with a simpler setup, presenting a tele-rehabilitation approach.

- **Joint stretching device**

  The authors present a study [Selles et al., 2005] with a 1 DoF ankle stretching device in the sagittal plane (see Figure 1.14) and one patient. The patient is asked to be totally passive, to avoid resistance against the movement of the robot. The aim of the therapy is to move the ankle of the patient, at a speed dependent on the resistance: the higher the resistance, the lower the speed. The maximum permissible torque is set by the therapist at the beginning of the training, and

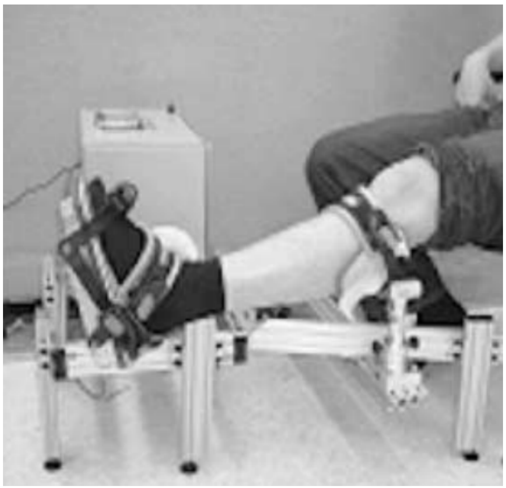


FIGURE 1.14: Joint stretching device [Selles et al., 2005].

once it is reached (it correlates to a maximum level of spasticity) the robot stops and the training finishes. There is no visual feedback.

- **Intelligent stretching device**

  In this study [Zhang et al., 2002], the authors performed a very similar treatment to that of the previous point, but with several subjects, with a similar device.

- **Assisted Movement With Enhanced Sensation (AMES)**

  In this study [Cordo et al., 2009], the authors present a 1 DoF (sagittal plane) device (see Figure 1.15), able to provide vibratory stimulation. The robot imposes a constant speed stretching movement at a fixed range of motion (ROM), asking the patient to be cooperative following the movement, and providing vibratory feedback on each change of direction at the antagonistic muscle mimicking the stretch reflex response.

FIGURE 1.15: Assisted Movement With Enhanced Sensation (AMES) [Cordo et al., 2009]. (Permission is granted at no cost for use of content in a Master's Thesis and/or Doctoral Dissertation.)

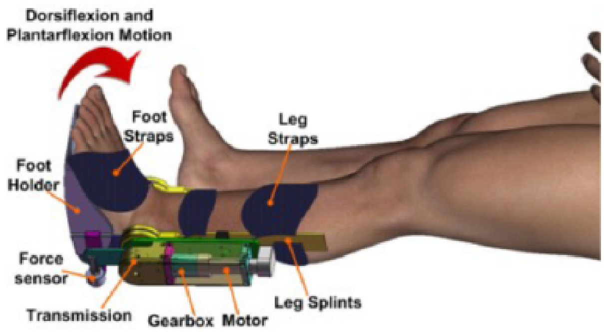


FIGURE 1.16: Wearable rehab robotic device [Ren et al., 2011]. Copyright ©2017, IEEE

There is no visual feedback either to the patient or the clinician.

- **Wearable rehab robotic device**

  In the study by Ren et al. [Ren et al., 2011], the authors present the design, development and testing of a 1 DoF (sagittal plane) device (see Figure 1.16) with the following features: 1) ability to follow patient's free movement; 2) possibility to assist the patient if needed, and resist to enhance muscle activation; and 3) the device is able to stretch the ankle. Features 1 and 2 are combined in the playing mode, where the patient is asked to perform the required movement for the game, and the error to the target is measured, and assisted or resisted if needed. Feature 3's implementation is similar to the previous studies: the aim of the therapy is to move the ankle of the patient, who is passive, at a speed dependent on the resistance: the higher the resistance of the ankle (directly related to the spasticity), the lower the speed.

- **Anklebot**

  Forrester et al. present in this study with the Anklebot [Forrester et al., 2011] a treatment coupled with a simple video game. The device is a 1 DoF (sagittal plane) robot able to provide assistance when needed. The patient is asked to move the foot in order to reach a target on the screen (see Figure 1.17), and if he/she is unable to reach it by own means, receives assistance from the robot proportional to the error to the target.

1.4 Conclusions

Previous pages have provided a brief explanation on how the gait is originated, which are the different mechanisms involved in the process, and the main alterations that a person may suffer such as paresis, muscle weakness and lower limb paresis, as a consequence, among others, of stroke or spinal cord injuries. Multiple pathologies, with high prevalence in today's society, have been described that limit motor capacity.

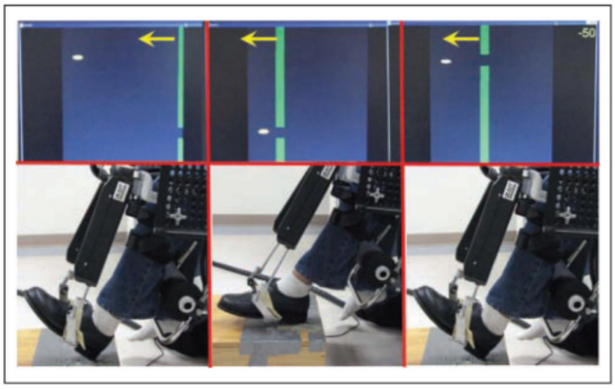


FIGURE 1.17: Anklebot exoskeleton with the video game designed for this study [Forrester et al., 2011]. (Permission is granted at no cost for use of content in a Master's Thesis and/or Doctoral Dissertation.)

Furthermore, this chapter has evidenced that human gait is much more than only the function that allows ambulation. It is a fundamental function for the integral development of humans from the very first years of life, since it influences all daily living activities, in the personal, work and familiar aspects. It allows interaction with the environment, but also constitutes a non-verbal communication mode, through which ideas or mood can be transmitted. Hence, the total or partial loss of mobility conditions the human not only in a physical dimension, but also at psychological and cognitive levels, in addition to the economic implications that this implies in the high health costs that it entails.

This work has been mainly developed in the framework of the BioMot [Moreno et al., 2014] project, whose approach was to provide improved interaction between the exoskeletal and human body structures in both behavioural and biomechanical dimensions, in both healthy and pathological conditions. The main objective of the project was to improve existing wearable robotic exoskeletons exploiting dynamic sensorimotor interactions and developing cognitive capabilities that can lead to symbiotic gait behaviour in the interaction of a human with a WR. In this line, the use of tacit learning [Shimoda and Kimura, 2010, Shimoda et al., 2010, Matsubara et al., 2006, Liu et al., 2007, Gibson, 2014] was proposed as a ways of promoting the adaptation of the robot both to the user/patient and to the environment, to provide a reliable interface between both agents.

Chapter 2

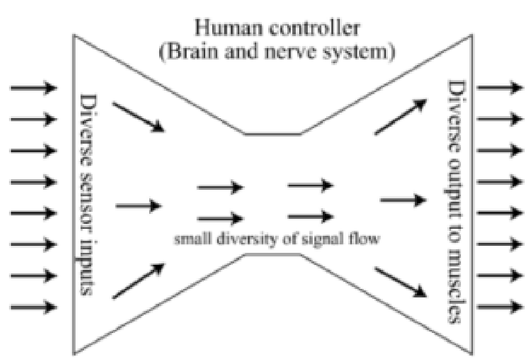
Exploration of the technology

In this chapter I expose the explorative journey before the development of the platform subject of this thesis, through the different components and prior developments to master the technology involved in the work. In the BioMot project [Moreno et al., 2014], we adapted the tacit learning algorithm [Shimoda and Kimura, 2010, Shimoda et al., 2013] from bipeds to exoskeletons [Shimoda et al., 2015], in section 2.1, and proposed the concept of tacit adaptability (TAd) with position controllers. Once we had access to the Mechanically adjustable compliance and controllable equilibrium position actuator [Van Ham et al., 2007], MACCEPA, (technology described in section 2.2), we proceeded to implement the adaptation of TAd and position controllers to this variable stiffness actuation based actuator, testing its behaviour on the testbench [Asín-Prieto, 2016a, Asín-Prieto et al., 2017d, Gonzalez-Vargas et al., 2017] (presented in section 2.3); and the first experiments of TAd on healthy individuals walking on a treadmill [Gonzalez-Vargas et al., 2017] (presented in section 2.4).

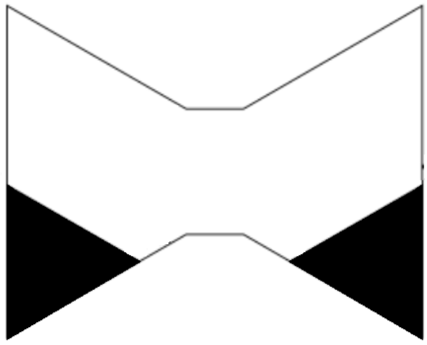
2.1 Translation of tacit learning (TL) concept from bipeds to exoskeletons: the concept of tacit adaptability (TAd)

In order to support humans' behaviours by using exoskeleton robots, how to decode the wearers' motion intention is one of the most important factors. Joint stiffness of the exoskeleton robot is one of the most important factors to support bipedal walking.

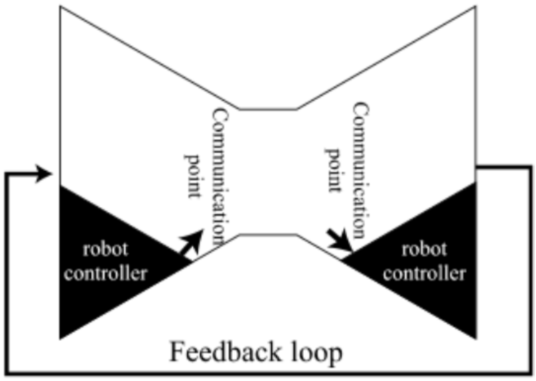
It is said that biological control systems can be modeled as a bowtie structure [Csete and Doyle, 2004, Alnajjar et al., 2015] described in Figure 2.1(a). Bowtie structure represents the essence of biological control systems where there are a great diversity of inputs and outputs while a smaller diversity of protocols is used to connect outputs and inputs. The inputs represent the sensor signals and the outputs, the signals to the muscles. In the case of the patients who need orthotic or prosthetic devices to enhance



(a) Bowtie structure representing the biological control structure.



(b) State when we lose parts of our bodies.



(c) Proposed idea of controller to adapt exoskeleton robot motions to humans' motions.

FIGURE 2.1: Bowtie structure.

or replace a compromised or lost function, bowtie structure is described in Figure 2.1(b) where some of the parts both in inputs and outputs are missing. Our idea to synchronize the patient control systems and the exoskeleton robot controller was the use of the robot controller at the compromised points.

To develop the robot controller that can be placed at these missing parts of human's controller as described in Figure 2.1(c), the controller must have the following two features:

1. Data analysis structure: the controller should communicate with the human controller at a higher level than the output from the human controller, such as electromyography (EMG) or joint angular position.

2. Adaptive behaviour to environment through interactions: the controller should adapt to both the human controller and the environment.

The first feature is required to know the motion intention at the appropriate level. In a previous study for the development of the forearm prosthesis [Iwatsuki et al., 2014], for instance, shoulder and elbow joint angles were measured to know how much the user wanted to rotate the wrist joint of the prosthetic arm.

The second feature is required according to the biological feature where the adaptation to the environment can be observed in the various levels of the brain through body/environment interactions. To synchronize to human's controller, the robot controller should be adapted to the other parts of the brain and the environment.

We proposed the use of the biomimetic learning architecture called TL, developed by Shimoda et al. [Shimoda and Kimura, 2010, Shimoda et al., 2013]. TL can tune the roughly defined robot behaviours to the sophisticated ones that are adapted to the environment, by mimicking the already mentioned features of biological controllers for the synchronization between robot and human: data analysis structure and adaptive behaviour to environment through interactions.

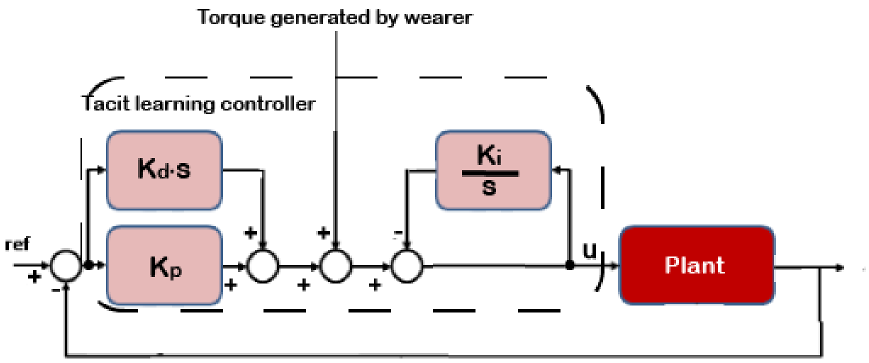
2.1.1 Materials and methods

2.1.1.1 Experimental platform

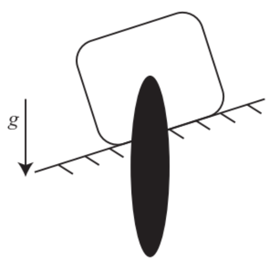
This experiment was performed with the H2 exoskeleton [Canela et al., 2013, Bortole and Pons, 2013, Bortole et al., 2015], connected via CAN bus communication to a CAN-enabled laptop running Linux and executing the control algorithm. We developed, prior to performing the translation to exoskeletons, a method to customize gait trajectories based on walking speed [Asín-Prieto et al., 2014b, Asín-Prieto et al., 2014c], and adapted an algorithm to detect potential falls [Asín-Prieto et al., 2015b, Asín-Prieto, 2015, Asín-Prieto et al., 2015a], with the aim of optimizing the integration of the human-robot system and ensuring the safety for the subjects.

2.1.1.2 Description of the algorithm

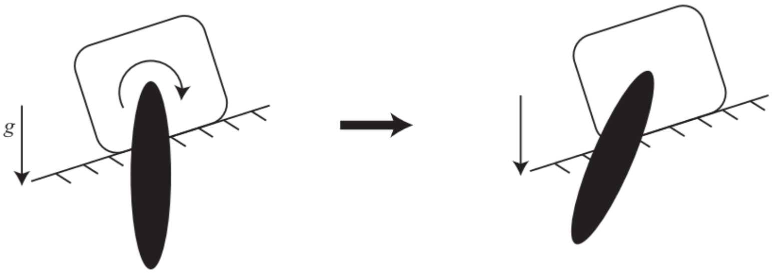
The human controller of the patients who need the exoskeleton robot support is described in Figure 2.1(c) where some of the parts of the human controller are missing. These missing parts imply that not only the actuators or the sensors but also the computation processes to integrate the sensor signals to the semantic signals or to decompose the semantics signal for each actuator signals may be missing. Placement of the artificial controllers, including such computational processes, is one of the interesting methods to design the controller for controlling the exoskeleton robot. The controller placed on the missing part can communicate with the human controllers in two ways. The first communication point inside the controller as described in Figure 2.1(c), implies that the robot controller and the human control system should be communicated with the semantic signal that is decoded from biological signals. The role of this communication is to provide the behaviour purpose to the controller.



(a) Block diagram of proposed controller.



(b) Posture where the joint angle is followed to the direction of gravity.



(c) Posture where the joint angle is followed to the wearer's exerted torque.

FIGURE 2.2: Proposed controller and behaviour.

The other is indirect communication through physical interactions. This is used to adapt the robot motions to the environment and human's motions by TL using the interaction torque. Therefore, bidirectional communication is required at this level. We used the controller shown in Figure 2.2(a) for stiffness tuning. This controller can change the joint stiffness by tuning the integral gain K_I. We implemented this controller for H2 and asked the healthy subject to bend his knee joint. Figures 2.3(b) and 2.3(c) show the results of collecting EMG signal of rectus femoris (RF) muscle and the joint torque respectively. This controller can be described as follows:

$$\tau = -K_P\theta - K_D\dot{\theta} - f \tag{2.1}$$

$$f = K_I \int \tau dt \tag{2.2}$$

Here, τ and θ imply the joint torque and the joint angle, respectively. K_P, K_D and K_I are the control gains.

2.1.1.3 Participants

Two healthy subjects with no previous brain injuries were enrolled for this experiment: one for sub-experiment 1 (one joint stiffness tuning); and one for sub-experiment 2 (joint stiffness tuning while walking).

2.1.1.4 Task description

In a previous study [Shimoda et al., 2012], Shimoda et al. showed that this controller can make the robot joint follow the direction of gravity as illustrated in Figure 2.2(b). When we apply this controller to the exoskeleton joint, not only the gravity but also the torque created by the wearer influence the joint. In this case, the joint angle is controlled to follow the wearer's torque as shown in Figure 2.2(c), reaching very low joint back-drivability. We used in this study the H2 exoskeleton, and it is noteworthy to mention that the intrinsic joint back-drivability is very low, such that almost 40 Newton·metre (N·m) external torque is needed to move the joint.

In this study, we performed trials with the subject in two different sub-experiments.

Sub-experiment 1: One joint stiffness tuning In this sub-experiment, we tested the joint stiffness turning by the proposed controller through body/exoskeleton interactions, with the subject wearing H2 and sitting. In this experiments, we focused on the right knee joint motions. $K_P = 20.0$ and $K_D = 20.0$ were used for the right knee control. Three different values for $K_I : 0.1, 0.05$ and 0.02, were used to change the stiffness.

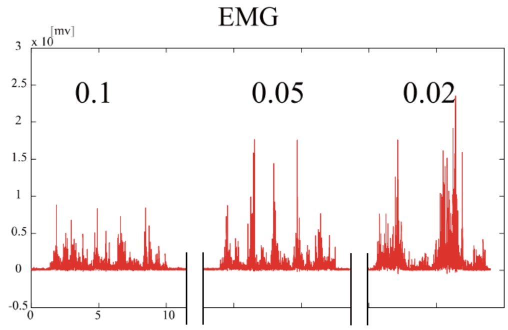
Sub-experiment 2: Joint stiffness tuning while walking In this sub-experiment, we set the same controller to the all joints of H2 and asked the subject to walking wearing H2. Three different values for $K_I : 0.1, 0.07$ and 0.05, were used to change the stiffness.

2.1.2 Results

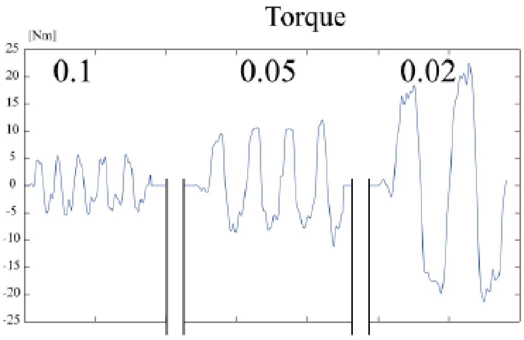
Sub-experiment 1: One joint stiffness tuning The experimental results are shown in Figures 2.3(b) and 2.3(c). In the case of the largest gain $K_I = 0.1$, *i.e.* lowest joint stiffness, the subject moved his knee joint smoothly with low EMG activation of RF. The maximum exoskeleton joint torque was 1.0 N·m. The EMG results and the exoskeleton joint torque showed that the joint stiffness got larger as the integral gain K_I got lower.

Sub-experiment 2: Joint stiffness tuning while walking In the case of $K_I = 0.02$, that was used in sub-experiment 1, the stiffness was so high that the subject could not walk. The right knee joint torques during walking are illustrated in Figure

(a) Overview of One joint stiffness tuning experiment.



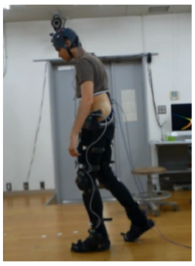
(b) EMG of rectus femoris muscle during experiments. When we used the larger integral gain, EMG got smaller suggesting the joint stiffness got smaller.



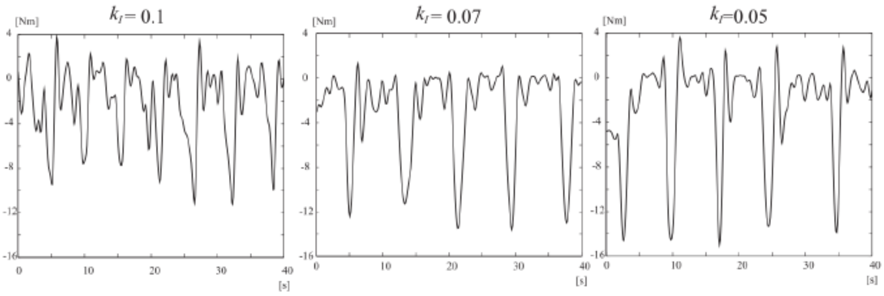
(c) Knee joint torque of H2 during the experiments. The results also showed the joint stiffness was tuned by changing the integral gain.

FIGURE 2.3: Sub-experiment 1 results.

2.4(b). Another important result from this experiment was the change of walking speed depending on the joint stiffness. The subject walked at 2.0 s per step in the case $K_I = 0.1$ while, he walked at 4.2 s per step for of $K_I = 0.05$.



(a) Overview of Joint stiffness tuning while walking experiment.



(b) Change of right knee joint torque depending of integral gain during walking with H2.

FIGURE 2.4: Sub-experiment 2 results.

2.1.3 Conclusions

To support the motions by using exoskeleton robots, the brain and robot controller should be well synchronized for a better support. From the results of the first sub-experiment, we concluded that the controller proposed in Figure 2.2(a) can tune the joint stiffness through body/robot interactions. The important feature of this controller is that the ability and transparency to follow the external torque is tuned via the gain of the integrator. When the gain becomes larger, the joint follows the external torque more easily, and vice versa. When the robot joint follows the external torque easily, we can assume lower stiffness of the joint.

From the second sub-experiment, the results also suggested that the stiffness tuning could be used to tune the walking speed.

These results showed that the proposed controller successfully tuned the joint stiffness by tuning the integral gains as was the case with the one joint experiments. We named this modification of the algorithm tacit adaptability since it allows an automatic adaptation of the exoskeleton control in real-time.

2.2 Mechanically adjustable compliance and controllable equilibrium position actuator, MACCEPA

This section presents the MACCEPA concept actuator, together with the frame and mechanical structure, and a description of the control.

MACCEPA [Van Ham et al., 2007] is a torque-controlled variable stiffness actuator (VSA) working as a torsion spring that allows independent control of equilibrium position and joint stiffness. Different realizations of the MACCEPA concept have been successfully applied in bipedal walkers [Huang et al., 2013], prosthesis [Flynn et al., 2015], stationary gait rehabilitation robot [Grosu et al., 2017] and a mobile sit-to-stand exoskeleton [Junius et al., 2014].

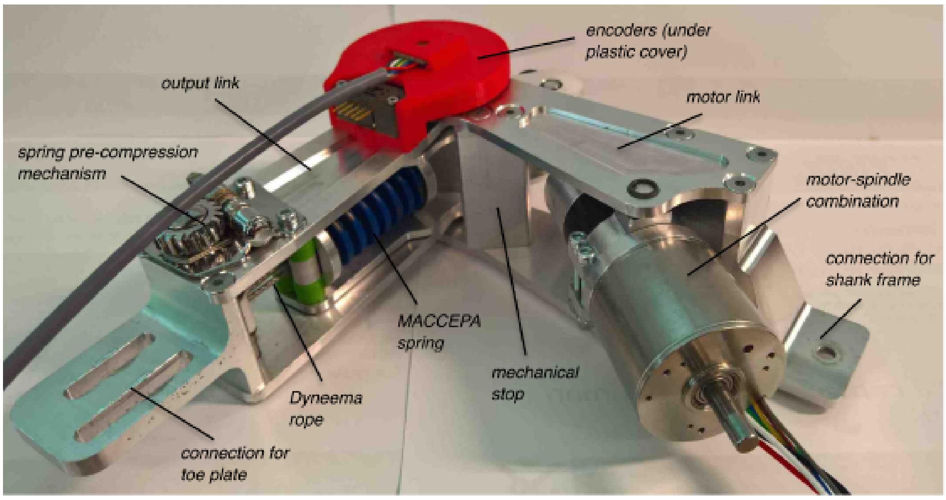
2.2.1 Mechanical structure

The shape of the actuator is guided by an anthropomorphic design approach, leading to revolute joint-actuators providing a torque in the sagittal plane. The actuators are designed with the goal of providing the same peak torque of minimally 50 N·m. This value comes from a capability gap analysis conducted within the BioMot project (the capability gap is the difference between the torque provided by a healthy and impaired subject). Actuator design parameters and drive-train components were all obtained from a simulation study performed in MATLAB, where energy requirements of the actuators to deliver both natural [Winter, 1991] and patients' walking patterns were minimized.

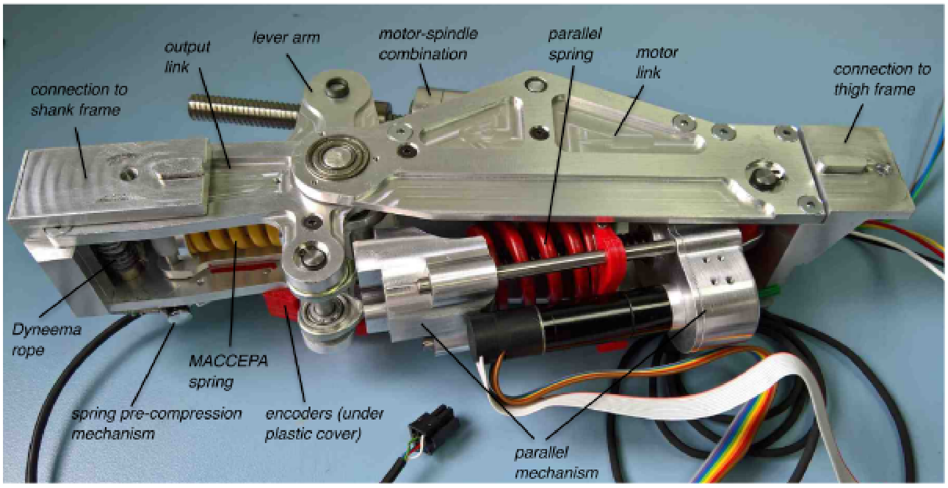
Spring pre-compression in the MACCEPA can be changed manually by means of a simple mechanism that proved to be robust and stable across different conditions. This, together with the spring being inside the Lever Arm (LA), allowed the actuators to be made small and compact.

The actuator consists of two distinctive parts - the motor side and the output side. The motor side houses a motor-spindle combination, while the output side houses LA, MACCEPA spring and spring pre-compression (P) system. The spring is inside the LA and there is a worm-gear pre-compression mechanism with Dyneema rope. Two encoders are used per actuator - incremental optical and absolute magnetic for measuring the biological angle (angle between two leg segments, called Fixed Link - FL) and spring deflection angle (angle between the actuators' LA and Output Link (OL), α), respectively. The motor is rigidly connected to the LA which is connected to the FL via the spring. LA and FL move with respect to OL. If the motor is set to a specific position, the user is still able to rotate the joint by compressing the spring, which allows to approximate the interaction force between the user and the actuator by measuring the resulting length of the spring (α angle). The actuators' ROM is limited by mechanical stops, and peak torque outputs are able to provide kinematically unobstructed fully-assisted motion at the knee joint and partially assisted at the ankle. Figures 2.5(a) and 2.5(b) depict the ankle and knee actuators respectively.

The frame and cuffs were designed with the aim of building a lightweight (less than 3 kg), comfortable and easily adjustable low-profile structure. To do so, the frame is built using spring-steel plates whose profile is chosen so as to be stiff in the sagittal plane, and flexible in the other two planes, thus minimizing the constraints the frame puts onto the human wearer. For practical, and frame's structural integrity, reasons, two sets of plates, different in length, were designed per leg segment, resulting in a total leg segment adjustability in between 0.35 and 0.45 m. The frame's height adjustability and the steel plates' replacement are simplified by using a minimal set of easily reachable same-size screws. Each plate is fixed to the respective actuator at one end, while having a groove towards the other end to allow adjustability. Figure 2.6 shows frame-cuffs setup of one leg segment. As seen in Figure 2.6, two cuffs are used per leg segment, one being at the back and another one at the front part of the segment. This way, the biggest torques exerted on the human wearer are transmitted by pushing, rather than by pulling on the cuff. The half-moon shape of the cuffs and a 3D printed flexible structure makes them easily adjustable to the user's leg shape. In order to fix the cuffs to the user's legs, an easy-to-use BOA closure system is employed. Another level of the cuffs' adjustability comes from the L-shaped spring-steel plates used to connect the cuffs to the frame, since these plates can be adjusted in both sagittal and frontal planes.



(a) Realization of the spindle-driven MACCEPA for the ankle joint. The lever arm ROM, if attached to a human as intended, is 32 degrees in plantarflexion and 21 degrees in dorsiflexion. The weight of the actuator is 1.18kg.



(b) Realization of the spindle-driven MACCEPA for the knee joint. The lever arm ROM is 2 degrees in extension and 90 degrees in flexion. The hyper-extension angle can be decreased if necessary. The weight of the actuator is 1.57kg.

FIGURE 2.5: Ankle and knee MACCEPA actuators. Copyright ©2017, IEEE

The footplate has several distinctive features in order to allow a natural and stable walking pattern when used over ground, while being able to transmit the required torques and adjust to the different users. To prevent the flat foot-drop after the heel strike, the footplate is divided into the toe and the heel plate. Both plates are slightly bent up at one end, in order to follow natural foot roll (see Figure 2.7), and are built in 2 millimetres (mm) thick spring-steel with a thin rubber underneath, which makes them slim and comfortable, yet durable enough to transmit the required torques. Furthermore, due to the adaptability of both plates in both axes of the sagittal plane [Moltedo et al., 2016], people of different foot sizes can wear the exoskeleton, provided they fit the wearer's height constraints. Finally, the adjustability of the foot plates is made simple by using a minimal number of easily reachable same-size screws, and a combination of easy-to-use Velcro and BOA straps.

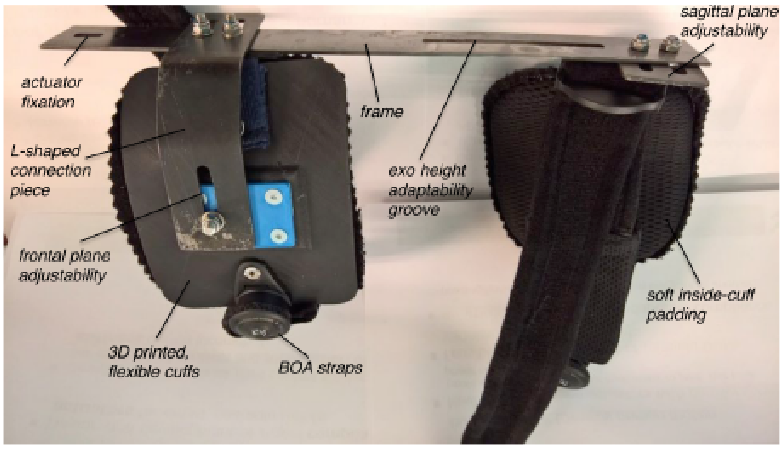


FIGURE 2.6: The frame plate and cuffs of one leg segment. Each leg segment has two cuffs placed at the opposite side of the segment in the sagittal plane to decrease the torque transmission losses and increase comfort. Cuffs are flexible and their position is adjustable in both sagittal and frontal planes. The frame's directional flexibility allows more natural gait pattern by providing passive DoFs in addition to the active ones. Passive DoFs allow limited deflection, yet sufficient to allow more natural gait. Copyright ©2017, IEEE

2.2.2 Electromechanics

The motor that actuates the module is a BrushLess Direct Current (BLDC) motor by Maxon, model EC-i 40, with 40 mm of diameter and 70 W of power (see Figure 2.8(a)). This motor is attached to a trapezoidal spindle to transform the rotating to linear motion. This trapezoidal spindle is also manufactured by Maxon, model GP 32 S, with 32 mm of diameter (see Figure 2.8(b)).

The electronic part of the actuators is constituted by a custom designed and developed dsPIC-based driver board (Secondary Processing Unit, SPU, see Figure 2.9(a)) and one controller board (BeagleBone Black board, BBB, `https://beagleboard.org/black`),

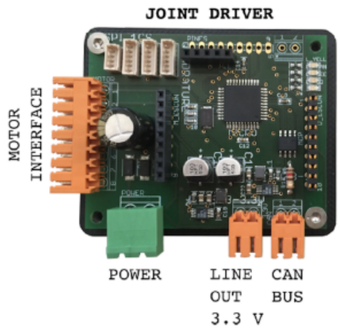
FIGURE 2.7: The plates have a low footprint and are easily adjustable to different users. Two BOA straps are used at the heel plate, and a single Velcro strap at the toe plate. Both plates are slightly bent up on one side - toe plate at the toe side, heel plate at the heel side, to allow a more natural walking pattern. Intermediary links and carriage screws are used to fix the plates to a desired position with respect to the ankle actuator (and thus ankle joint axis). Copyright ©2017, IEEE

(a) EC-i 40 motor.

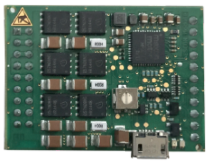
(b) GP 32 S trapezoidal spindle.

FIGURE 2.8: Motor and spindle.

connected via a CAN-bus network. The SPU, is responsible of running the control algorithms of the actuated joint, and of sensor data acquisition (angular encoders, force resistive sensors, contact sensors, etc), sending control output every three milliseconds to the actuator. The data from the SPU are then gathered, packed and sent via the CAN communication channel towards the BBB, in charge of non real-time tasks and communications, at 100 milliseconds intervals. The SPU includes a commercial driver: an ESCON 50/5 driver board (see Figure 2.9(b)). For CAN communication, we developed a CAN cape expansion board, including the necessary transceivers. Figure 2.10 shows the BBB together with the CAN cape.



(a) BioMot SPU.



(b) ESCON 50/5 driver board.

FIGURE 2.9: BioMot SPU board and driver.

To select the BBB board, we took into account that one of the main goals for the board was the integration between all the devices forming the data acquisition system. In order to achieve such objective, the device needed to support analog communications, have a network interface, and particularly critical was the availability of a CAN interface since it was the connection used by the electronic boards controlling the joints for fast communication. Using a well-developed and open-source operating system as Linux allows for costs reduction and makes a large amount of software and libraries available for development. Since the board needed to be set-up for portability, low power consumption was an essential requirement.

There are two sensors, as already pointed before: an optical and a magnetic encoder. The optical encoder (see Figure 2.11(a)) measures the angle between FL and OL, *i.e.* the ankle angle, and it is the model E6 by US Digital. The magnetic encoder (see Figure

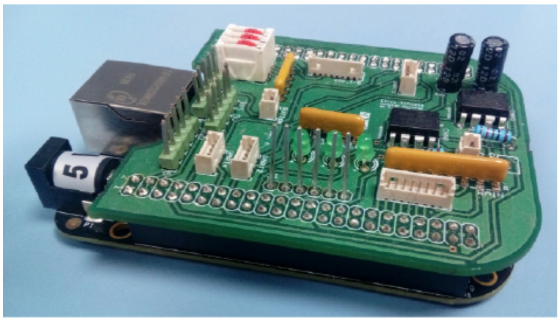
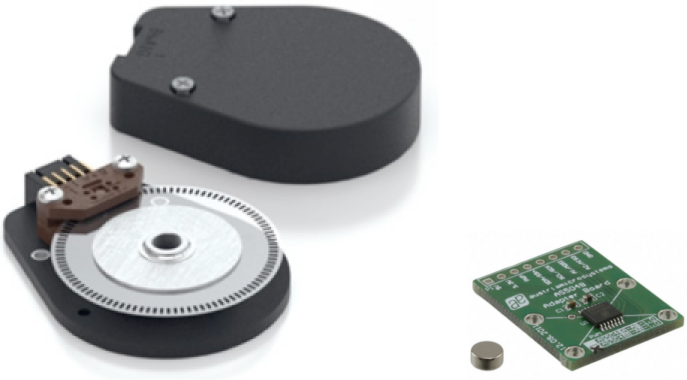


FIGURE 2.10: BeagleBone Black with CAN-cape expansion.

2.11(b)) measures the angle between FL and LA, α, and it is the AS5048A/B by Austria Micro Systems (AMS).



(a) Optical encoder. (b) Magnetic encoder.

FIGURE 2.11: MACCEPA actuator sensors.

2.2.3 Control

A regular position controller and a torque controller have been implemented in the actuator. However, MACCEPA's design allows it to be position-controlled prior to a compliant element, while acting as a torque source from the viewpoint of the joint [Grosu et al., 2017], and thus here I present the implementation of the torque controller, that relies on a position controller, and consequently the latter remains explained if the former is described. Torque mode is a low-level control approach in which the actuator tries to apply the prescribed resistive torque which the user feels by driving the exoskeleton. In the case of the MACCEPA, the proportional-integral-derivative (PID) controller works by imposing the needed deflection angle α, since MACCEPA's torque can be directly inferred from this angle. This is a straightforward approach since the deflection angle is directly measured by one of the encoders.

For the torque control, I bring back the basic concept of MACCEPA, recalling that it is a VSA that uses a linear spring whose resting length (pre-compression) can be changed. Although it uses a linear spring, from the joint point of view, MACCEPA

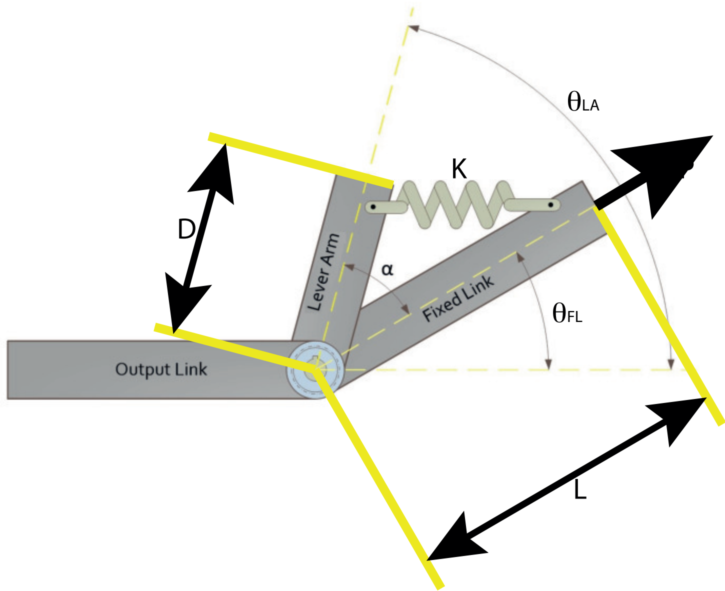


FIGURE 2.12: Model of MACCEPA actuator.

acts as a torsion spring due to its geometry and force (torque) transmission. The actual linear spring stiffness is predefined, as it is a physical property of the spring. However, its resting length can be changed, thus changing the behaviour of the actuator.

The MACCEPA acts as a torsion spring at joint level. According to Hooke's law, the torsion spring torque depends on a torsional stiffness and deflection angle. A property of the MACCEPA is that its torque-angle characteristic corresponds to a torsion spring characteristic. In other words, MACCEPA's deflection angle corresponds to a torsion spring deflection angle, while the slope of its characteristic corresponds to a torsion spring stiffness. By exploiting this property, a control approach is derived in which MACCEPA's LA is position-controlled prior to the compliant element, while the actuator acts as a torque source. From the MACCEPA formula [Van Ham et al., 2007], torque depends, apart from the geometry of the actuator (lengths D and L, refer to Figure 2.12) and linear spring stiffness (K), also on the spring pre-compression (P) and the torque angle, as seen in equation 2.3.

$$\tau_{MAC} = K \cdot D \cdot L \cdot sin(\alpha) \cdot \left(1 + \frac{P - |L - D|}{\sqrt{D^2 + L^2 - 2 \cdot L \cdot D \cdot cos(\alpha)}}\right) \tag{2.3}$$

The behaviour of the actuator can be approximated by a linear torsion spring at the joint level. Torsion spring torque τ_{ts} depends on the torsion stiffness K_{ts} and the deflection angle α (Hooke's law), as seen on equation 2.4.

$$\tau_{ts} = K_{ts} \cdot \alpha \tag{2.4}$$

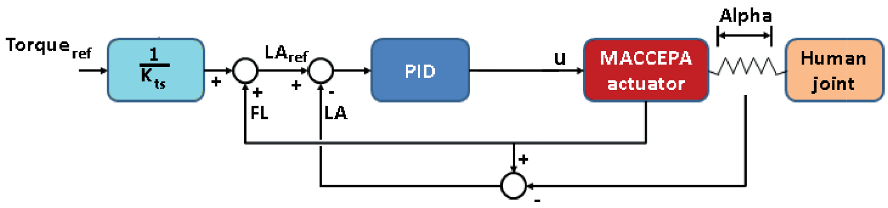


FIGURE 2.13: Low-level torque controller for the MACCEPA.

The pre-compression P of the spring can be controlled, rendering possible to control Hooke's constant of the virtual torsion system K_{ts}, and thus to obtain K_{ts} as a function of P: $K_{ts} = K_{ts}(P)$. Furthermore, $\alpha = LA - FL$, *i.e.* α is the deflection between the position of the robot (LA) and the biological ankle angle (FL) of the actual joint of the user. Consequently, by knowing a desired torque τ_{ref} coming from a high-level control layer, a desired LA angle can be extracted as seen in equation 2.5.

$$LA_{ref} = \frac{\tau_{ref}}{K_{ts}} \cdot FL \tag{2.5}$$

Thus, MACCEPA is position-controlled prior to the compliant element, but it acts as a torque source at joint level. Figure 2.13 depicts the resulting controller diagram.

In short, by using the information from MACCEPA encoders in real time, and characterizing the information on the relation between MACCEPA's spring pre-compression P and torsion spring stiffness K_{ts}, *i.e.* by obtaining $K_{ts} = K_{ts}(P)$, it is possible to turn MACCEPA into a torque source, without having a torque sensor in the system, all while employing a simple position control.

2.3 Translation of TAd from rigid to compliant actuators: testbench experiments

Section 2.1 has the description of the successful implementation of TAd to improve the adaptability of H2 stiff actuated exoskeleton. However, due to the rigidity of this exoskeleton, this adaptation was limited. Therefore, in this study, we modified the TAd algorithm to be used with MACCEPA actuator (already described in section 2.2). We tested the control strategy in two settings: one simulating the extreme case of a user unable to move, and the other one mimicking the interaction abled individuals.

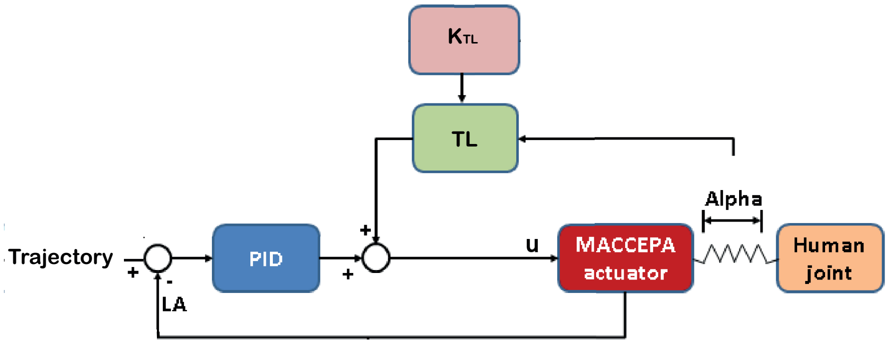


FIGURE 2.14: Block diagram of the implementation of the tacit learning concept for the MACCEPA. α represents the deflection between LA and FL.

2.3.1 Materials and methods

2.3.1.1 Experimental platform

The knee actuator was used for these experiments. In a real scenario with a subject wearing the device, OL should be attached to the thigh, while FL should be attached to the shank. In short, the MACCEPA has its motor rigidly connected to LA, which is connected to FL with a spring. LA and FL move with respect to OL. Figure 2.14 shows a block diagram of the system. As already shown in section 2.2.3, the interaction torque at the joint can be approximated by measuring the deflection (α) of the spring placed between the motor and the output link.

The system was powered with a 24 volts/300 watts power supply. A magnetic encoder measures α, what allowed us to infer the interaction between the user and actuator through the spring compression. An absolute optical encoder measures the angle on the user's joint. The data was acquired in a PC, running Simulink, with a PCI CAN card. We recorded 60 seconds per condition sampled at 200 hertz (Hz).

2.3.1.2 Description of the algorithm

TAd algorithm is shown in (Figure 2.14). This control strategy tries to automatically adapt a reference trajectory to the user's movement capabilities, by shifting the demanded position to an autonomously determined range in function of user induced constraints. Thus, the output of a position PID controller is modulated by an integral gain we call TAd constant (K_{TA}). Therefore, if the user is not able of realizing the trajectory, the output of the control adapts proportionally to the interaction torque between the exoskeleton and the user. This adaptation is important, since it will automatically reduce the force applied to the user. The response time of the adaptation can be modulated by changing K_{TA}.

The position PID controller was tuned using the Ziegler-Nichols method without any load at FL. It is important to notice that the loop is closed using the angle at the side of the motor (LA) and not at FL. This way, the spring absorbs small deviations of FL from the desired trajectory, effectively reducing its negative effect on the stability of the trajectory controller.

The output of the controller is adapted according to the measured α between the load at FL and the torque generated by the motor. This adaptation is given by a proportional and integrative term as defined in equation 2.6.

$$TL = K_P \cdot \alpha + K_{TA} \cdot \sum \alpha \tag{2.6}$$

Where the proportional constant K_P is chosen to reduce the perceived stiffness due to the static friction (or stiction) of the actuator. K_{TA} is the stiffness gain and defines the rate of adaptation of the output to the interaction forces. This variable is effectively changing the perceived stiffness of the joint by modulating how fast it minimizes the interaction torque. The values of this variable are normalized from 0 to 1.

Therefore, if K_{TA} is increased the control output will adapt faster to follow the torques produced by the user. This will result in a reduction of the measured interaction forces and therefore a more transparent movement. On the other side, if K_{TA} is decreased, the perceived stiffness of the joint is increased, driving the movement closer to the specified trajectory of the exoskeleton. In this regard, the tacit adaptability scheme can be used to expand the range of compliance of the actuator by modifying the value of K_{TA}.

The controller was programmed using MATLAB xPC target installed in a PC/104. The control loop ran at 1 kilohertz. The sensor data was transferred to a laptop computer using a UDP connection.

2.3.1.3 Participants

No participants were needed for the protocol of sub-experiment 1. Seven non-impaired subjects participated in the second sub-experiment. They were asked to repeat the movement for ten cycles for K_{TA} values of 0, 0.25, 0.5, and 0.7.

2.3.1.4 Task description

We performed two different studies on the testbench with MACCEPA actuator and TAd.

Sub-experiment 1: Static configuration We fixed the links (OL and FL) of the actuator to a rigid structure, and allowed the motor to move LA by compressing the

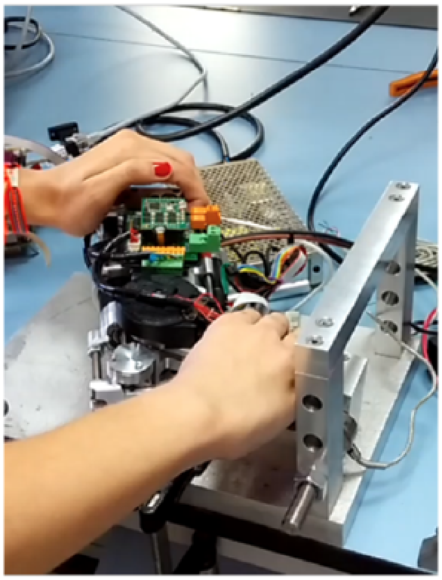


FIGURE 2.15: Static test of the experiment. One link of the actuator was fixed, allowing the subjects to move the other link. Copyright ©2017, IEEE

spring. The goal with this setup was to explore the adaptability of the controller to predefined reference trajectories. We proposed a condition to simulate the situation in which a user is not able to generate any limb movement. In our setup, the actuator was limited to the horizontal plane to avoid the effects of gravity. In this scenario, the mechanical compliance, given by the spring constant, absorbed some of the force that the motor applied to the simulated user's limb. Since the limb could not move as it was fixed in one position, TAd adjusted the reference trajectory, to further reduce the applied force. TAd controller was set to follow a 60 degrees sinusoidal trajectory (full range of motion of the knee actuator) at a frequency of 0.2 Hz. The range for α was determined by the spring stiffness. The actuator was fixed at three different joint angles (15, 30 and 45 degrees). We recorded LA and the controller output for 5 different K_{TA} values (0, 0.05, 0.1, 0.15 and 0.2).

Sub-experiment 2: Dynamic configuration This experiment was performed with the same setup as in the first study (section 2.3.1.4), but with the motor link (OL) free to move (Figure 2.15). The trajectory set to the exoskeleton was a square wave that ranged between 10 to 50 degrees, at a fixed frequency of 0.25 Hz. The pre-compression of the spring was set to 40 % (7.6 mm). Subjects were asked to move OL between 10 to 50 degrees at 0.5 Hz, double the frequency of the square wave set on the exoskeleton, using their hands. The subjects used an audio cue to time their movements at the desired frequency. The movements executed by the subject were in phase with the movements of the exoskeleton half of the time and out-phase the other half. This way, we could characterize the behaviour of the controller for different values of K_{TA}.

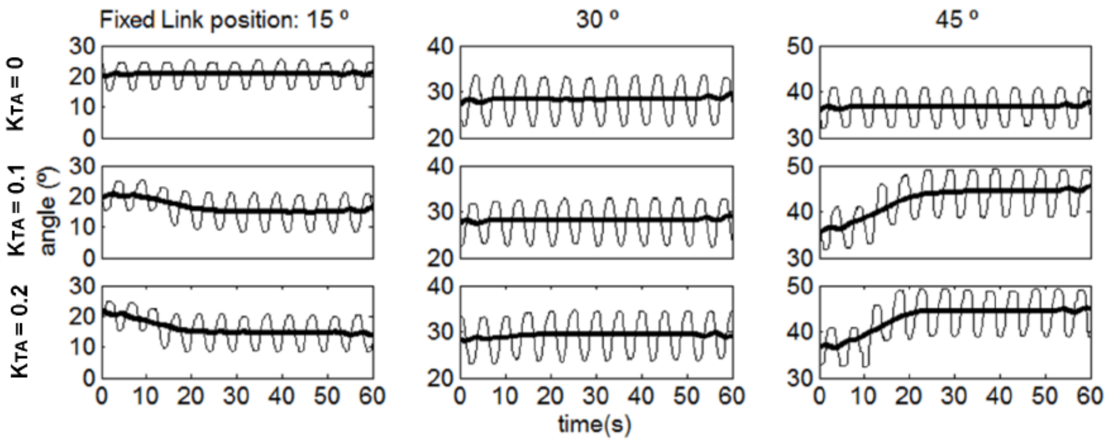


FIGURE 2.16: Comparison of α angle amplitude for K_{TA} values of 0, 0.1 and 0.2 during the experiment. α angle amplitude is represented with a slim line; the thick line shows the trend, calculated as the centred moving average (3000 points window over the 12000 points signal).

For this experiment, we measured the root mean square of α during the in-phase and out-phase movements. The α indirectly measures the interaction forces. Also, we recorded the maximum and minimum angles achieved by the subjects during the task. A Repeated Measurements ANOVA with the Greenhouse-Geisser correction was used to compare these variables between conditions. A Bonferroni post-hoc was used to compare the different values of K_{TA}.

2.3.2 Results

Sub-experiment 1: Static configuration Figure 2.16 shows the results on the evolution of α with different values of K_{TA}. When $K_{TA} = 0$, the behaviour was a pure PID control, thus no adaptation on LA position trend can be seen. When the K_{TA} took values greater than zero, TAd acted, and the sinusoidal signal was modulated in a way that the neutral position of LA was aligned with the position of FL.

Sub-experiment 2: Dynamic configuration The left plot of Figure 2.17 shows an example of the angles of the output link of the actuator (red) and the reference trajectory (black) for two different values of K_{TA}. Table 2.1 shows the average and standard deviation of OL angle for all subjects. When $K_{TA} = 0$, the subjects tended to overshoot from the expected angles (10 and 50 degrees) if the trajectories were in-phase. This was related to the fact that the motor was generating torque in the same direction of the subject; thus the movement was easier to achieve. However, when the subject's and the exoskeleton's movements were out-phase (moving in the opposite direction) the subjects had difficulties to reach the desired angles. This result was expected since the controller did not take into account the torque generated by the subjects and therefore was not adapting to their volitional control.

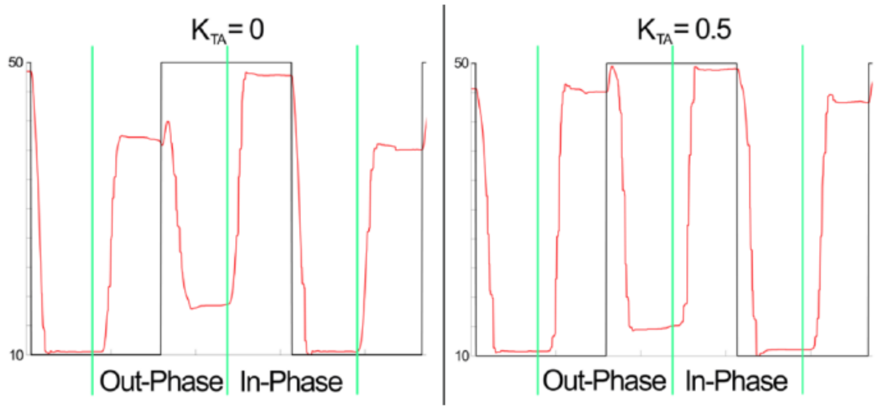


FIGURE 2.17: Squared wave trajectory set for the exoskeleton (black) and angle realized by the subject for $K_{TA} = 0$ and $K_{TA} = 0.5$. When $K_{TA} = 0$ it becomes more difficult for the subject to achieve the expected angles when the trajectories are out-phase. When $K_{TA} = 0.5$ the subject has more control to realize the expected angles during when the trajectories are out-phase. Copyright ©2017, IEEE

On the other hand, when $K_{TA} > 0$, the subjects were able to achieve the desired angles with less difficulty for both the in-phase and the out-phase movements. This shows a reduction in the stiffness of the joint. The right plot of Figure 2.17 shows a normalized example for the results at $K_{TA} = 0.5$. This can be noticed since the desired angles were closely approached during the task. A significant difference ($p < 0.05$) was found between the maximum and minimum angles achieved for $K_{TA} = 0$ and the rest of the values for the in-phase and out-phase movements.

Figure 2.18 shows the mean and standard deviation of the spring deflection during in-phase movements for different K_{TA} values. Also, Figure 2.19 shows the spring deflection values for the out-phase values. It can be noticed that for $K_{TA} = 0$ the deflection of the spring was significantly higher ($p < 0.01$) than for other values of K_{TA} for both in-phase and out-phase. This indicates that there were more interaction forces, and therefore, the actuator was stiffer. As K_{TA} was increased, the interaction forces were reduced. Also, when the movement was out-phased, the spring deflection was significantly higher ($p < 0.01$) than when the movement was in phase for $K_{TA} = 0$. During the experiments, the maximum interaction torque measured was approximately 12 N·m.

TABLE 2.1: Maximum and minimum values of the output link angle for different values of K_{TA} when the movement was in-phase and out-phase. The values show the angle in degrees and its standard deviation inside the brackets. Copyright ©2017, IEEE

K_{TA} Value		0	0.25	0.5	0.7
In-phase	Maximum	62.8 (2.9)	59.4 (4.5)	57.6 (6.1)	57.1 (5.6)
	Minimum	9.4 (4.7)	5.3 (6.9)	6.6 (7.5)	6.1 (6.3)
Out-phase	Maximum	48.12 (6.9)	54.9 (7.1)	52.5 (5.8)	51.1 (7.2)
	Minimum	21.1 (6.4)	10.9 (7.8)	11.3 (7.4)	9.7 (5.9)

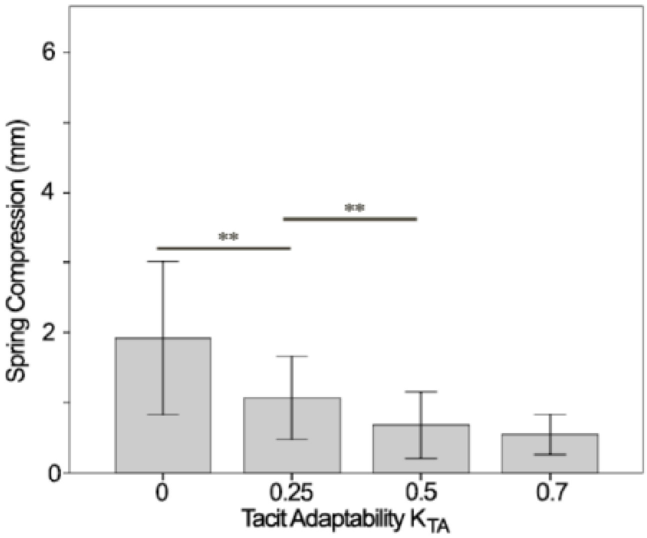


FIGURE 2.18: Mean spring deflection values for various values of K_{TA} in-phase movements. There is more interaction when $K_{TA} = 0$ and it is significantly different from the other conditions $K_{TA} > 0$. Copyright ©2017, IEEE

2.3.3 Conclusions

The preliminary results showed that using the TAd concept on a compliant actuator it is possible to modulate a fixed trajectory reference to adapt to the position limits that are induced by user's movement capabilities. We tested the control strategy in a setting that simulates the extreme case where the user is not capable of realizing any movement (sub-experiment 1), and then in a dynamic setup, mimicking interaction with able to move individuals (sub-experiment 2). When no TAd was used, we observed

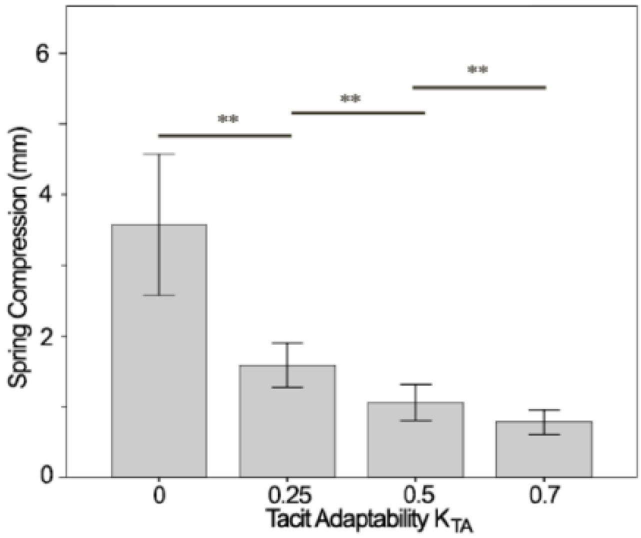


FIGURE 2.19: Mean spring deflection values for various values of K_{TA} out-phase movements. There is more interaction when $K_{TA} = 0$ and it is significantly different from the other conditions $K_{TA} > 0$. Copyright ©2017, IEEE

that the control output resulted in a stiffer behaviour of the actuator. On the other hand, a high K_{TA} resulted in a more compliant behaviour of the actuator. Thus, the adaptation was given by the compliance of the exoskeleton as well as by TAd. These results pointed out at the possibility to automatically adapt a fixed reference trajectory to the movement capabilities of the user by modulating the K_{TA}, and that the proposed controller could synchronize the volitional control of a person with a reference trajectory of an exoskeleton during locomotion.

2.4 TAd and MACCEPA: From the testbench to the treadmill

The main objective of the next study was to combine the technology of MACCEPA compliant actuator with the concept of TAd to improve the synchronization between the exoskeleton and the user during joint movements. With this study, we aimed at setting the base to develop an automatic shared control strategy capable of easily balancing the control burden between the user and the exoskeleton. To achieve this, we adapted the TAd controller to modify the joint stiffness of the actuator based on the interaction between the user and exoskeleton by accumulating the interaction signals between the exoskeleton and the user. In this way, we could combine the mechanical (intrinsic) and virtual (due to TAd) elastic characteristics of the actuator to minimize the interaction while still providing support for the user during locomotion.

2.4.1 Materials and methods

2.4.1.1 Experimental platform

We tested the behaviour of the controller during walking on a treadmill (Figure 2.20). For this test, we used the ankle actuators on both legs. Also, a force sensor placed on the heel plate of the actuator was used to reset the ankle trajectory at heel strike.

2.4.1.2 Description of the algorithm

The exoskeleton trajectory was generated using the method described in [Asín-Prieto et al., 2015b]. This method uses a spline approximation from experimental data of human lower-limb joints during walking. The generated ankle trajectory was calculated for each subject to walk at a speed of 1.5 kilometres per hour.

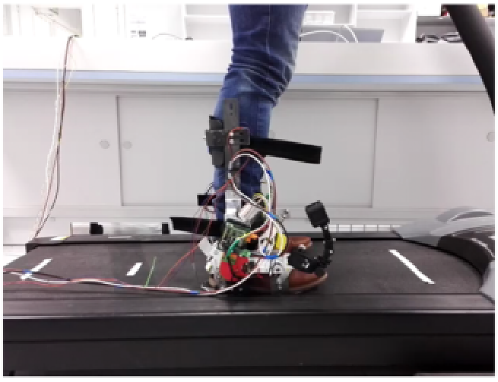


FIGURE 2.20: Walking test of the experiment. Both ankle actuators were fitted to the subjects, who walked on a treadmill with a speed of 1.5 kilometres per hour. Copyright ©2017, IEEE

2.4.1.3 Participants

Two non-impaired subjects were enrolled for this experiment.

2.4.1.4 Task description

During walking several values of K_{TA} were used. These values were normalized from 0 to 1, and increased for 0.1 every 30 seconds. When $K_{TA} = 0$ (highest stiffness), the control output did not have any input from the TAd. Therefore, the actuator forced the user towards the generated trajectory. On the other side, when $K_{TA} = 1$, the actuator worked as a zero-impedance controller, thus it followed the user's movement. The values in between, used the TAd to balance the input from the generated trajectory and the user's movements.

The subjects were asked to walk on a treadmill while the values of K_{TA} were decreased by 0.1 every 30 seconds. The subjects started the task with K_{TA} value equal to 1 (low stiffness). The interaction torque was measured as the root mean square value of the deflection of the spring over a walking cycle. This way, we could observe the change of the behaviour of the interaction forces for different values of K_{TA}. Also, it can indicate the influence of the exoskeleton generated torque and the volitional movement of the subject.

2.4.2 Results

Figure 2.21 shows the behaviour of the interaction forces of the right and left leg of both subjects during the experiment. The maximum interaction force exerted during the experiments was approximately 15 N·m, which corresponded to an α of 30 degrees at the fixed pre-compression. From the figures, it can be noticed that the interaction forces were considerably reduced when K_{TA} was increased. If K_{TA} was decreased, then

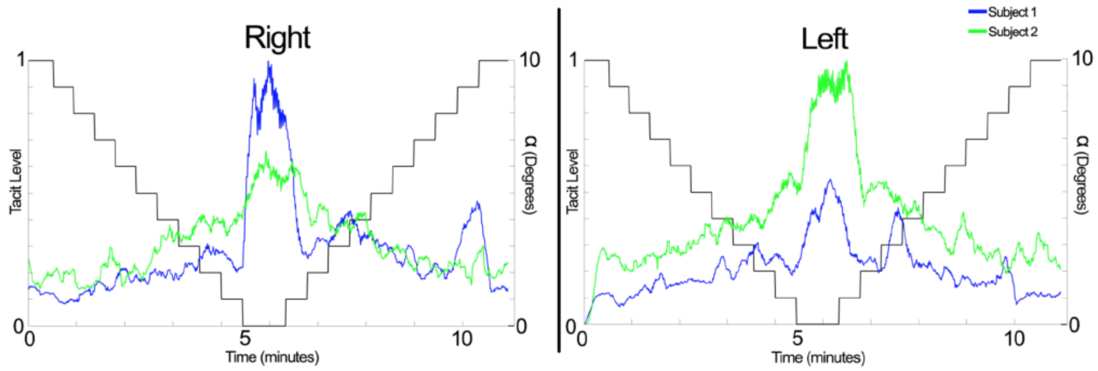


FIGURE 2.21: Normalized K_{TA} ramp and α for two subjects. As K_{TA} increases, the deflection decreases, thus there is less interaction at the joint. Therefore, the actuator output adjusted to the user's movements. The maximum exerted force was approximately of 18 N·m.

the movement of the subject became bounded to the trajectory of the exoskeleton. Therefore, the subject perceived the actuator to be stiffer and less responsive to his volitional movement. This forced the subjects to make a higher effort to adapt to the exoskeleton trajectory to keep walking without falling. Nevertheless, the compliance of the MACCEPA allowed the subject some freedom to move outside the exoskeleton's trajectory.

This result points out that the ankle joint movement was more restricted to the reference trajectory as K_{TA} was decreased. On the other hand, when K_{TA} was closer to 1, the user mainly controlled the movement, but as K_{TA} decreased the control was shared between the exoskeleton and the user. Therefore, the modulation of the actuator stiffness allowed a faster coordination between the exoskeleton and the user. However, if the stiffness was too high or too low, it became more difficult for the actuator to adapt to the volitional movement of the subject.

Results for other two different subjects and only for the left leg are shown in Figure 2.22. From the figures, it can also be noticed that the interaction forces were considerably reduced when K_{TA} was increased. This shows that the control strategy allowed the actuator to adapt the desired trajectory to the movements of the subjects. If $K_{TA} = 0$, then the subject was guided towards the desired trajectory. However, the mechanical elasticity given by the spring of MACCEPA allowed the subject some freedom to move outside this desired trajectory. This made it easier for the subjects to adapt to the fixed trajectory.

2.4.3 Conclusions

In rehabilitation, it is important to synchronize the control of the exoskeleton with the movement capabilities of a user to optimize the support to the movement while promoting an active participation of the user [Yan et al., 2015]. Therefore, the development of

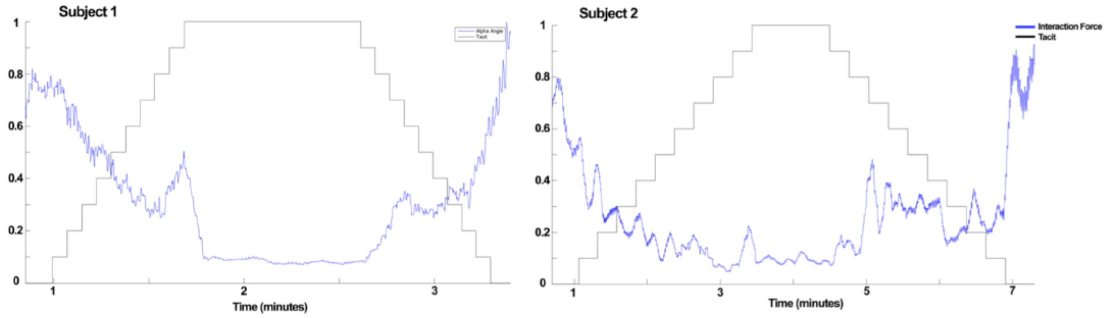


FIGURE 2.22: Normalized K_{TA} ramp and α for another two subjects and only left leg.

efficient exoskeletons requires the development of new mechanical and control strategies to cope with the biomechanical and neural characteristics of humans [Carpino et al., 2013]. In particular, the concept of embodied intelligence has resulted in the development of novel actuation systems capable of exploiting dynamic features of the task to reduce the burden on the controller. In this sense compliant exoskeletons (*i.e.* using series elastic actuators), are being used due to the capability to mechanically adapt to the user and the environment, greatly improving their usability and safety [Moltedo et al., 2017, Grosu et al., 2015]. For example, a compliant exoskeleton is capable of absorbing the shocks resulting from heel strike during gait or adapting to the different ground surfaces, without a complex set of sensors and control algorithms.

State-of-the-art control strategies vary accordingly to the intended application and structure of the exoskeleton, as well as with the instrumentation necessary for sensing the state of the human-exoskeleton system [Chen et al., 2016, Tucker et al., 2015]. However, it is important to develop shared control strategies that automatically balance the control burden between the user and the exoskeleton to optimize the intervention [Tucker et al., 2015].

In this study, we implemented a behaviour adaptation control based on TAd [Shimoda et al., 2013] using a compliant actuator [Moltedo et al., 2017]. This control architecture allowed modulating the stiffness of the actuator without complex torque sensors and complex human or interaction models. The preliminary results show that the proposed controller can synchronize the volitional control of a person with a reference trajectory of an exoskeleton during locomotion.

During the walking test, all subjects agreed that they felt comfortable when walking at K_{TA} values higher than zero, at mid values they perceived the exoskeleton contribution, but it was not impeding their locomotion rhythm. This agrees with the interaction values presented in Figures 2.21 and 2.22, which were in general low values. Therefore, even if the reference trajectory does not take into account the variability of the step length or the speed that is always present when walking, the proposed algorithm could boost the capacity of the compliant actuator to cope with these changes by accumulating the interaction signals between the exoskeleton and the user. Subjects agreed that when

$K_{TA} = 0$, the actuator felt stiffer and that they had more difficulty to keep their walking rhythm. However, thanks to the compliant actuator, they were still able to maintain their balance and walking rhythm. These observations are clearly shown in Figures 2.21 and 2.22, since at this time the interaction was significantly higher.

This implementation was aimed at establishing a lower-level controller that could be modulated to balance the shared control between an exoskeleton and its user during locomotion. Therefore, to apply this architecture to a real rehabilitation scenario, there was a need to develop a system that automatically takes care of setting the joint stiffness depending on the capabilities and needs of a patient during locomotion.

In this context, K_{TA} could be modulated based on biometrics such as attention level on the task [Asín-Prieto, 2016b]; or internal metrics of the therapy (concept in which we based the design of the rehabilitation tool), *i.e.* the performance results of the patient, to find the minimal support needed for the patient to achieve the movement task. Therefore, if the patient is not able to realize the task, or the performance is low, then K_{TA} could be decreased. This will increase the contribution of the exoskeleton to the movement. In the case that the performance was high, then K_{TA} could be increased, which would give more responsibility to the patient, reducing the support and promoting the patient volitional control. A significant advantage of combining TAd and a compliant actuator is that it increases the dynamic features of the actuator. Therefore, it can act and react better to external perturbations or the intrinsic variability of humans (*e.g.* variable step length or the perturbation given by the heel strike). Therefore, the system could be used to adjust the coordination between the exoskeleton and the human progressively. This way, by adjusting K_{TA}, the patient movement can be progressively guided towards the desired movement profile.

2.5 Conclusions of the chapter

In this chapter, I have covered the explorative journey followed before the development of the proposed rehabilitation robotic tool. First, I have cursorily presented the robotic tool used for the development: MACCEPA.

Then I have shown the study we have published around the H2 robotic exoskeleton, towards gaining the knowledge needed for the accomplishment of the objective of the thesis, before we were delivered the robotic actuators to be used in the final work: the MACCEPA. With the H2 exoskeleton, we performed the first approach of the tacit learning algorithm for wearable robots: tacit adaptability. I have provided evidence on how this algorithm was able to adapt a rigid position controller with rigid actuators to user intentions, thus providing joint stiffness tuning.

With the MACCEPA, we translated TAd algorithm to be used with compliant actuators. I have presented the studies we performed with this approach, also applied to a position controller on MACCEPA, on the testbench mimicking static and dynamic conditions, with different TAd values; and with healthy users walking on the treadmill, also with different fixed TAd values.

Chapter 3

Modulation of muscle activity applying novel force paradigms

This chapter describes the experiments around the development of the T2 phase centred protocol. T2 rehabilitation phase is focused on the preparatory exercises for gait training. Thus, in these experiments, the robotic tool was used with the patient standing, body weight support (BWS)-like, and provided two different gait rehabilitation training approaches in healthy individuals. These experiments were proposed to explore the application of torque with the developed robotic tool, proposing two novel paradigms.

Neural impairments usually lead to inappropriate muscle activation and, consequently, to impaired motor function [Safavynia et al., 2011, Cheung et al., 2012]. One common disability that follows neurological injury is disrupted walking function due to impaired dorsi-plantarflexion. For instance, some incomplete spinal cord injury (iSCI) patients leave the ankle dorsiflexed during the stance phase of walking, which compromises an effective push-off of the foot [Ditunno and Scivoletto, 2009]; other iSCI patients walk with excessive plantarflexion and present impaired foot contact [Van Der Salm et al., 2005]. Some stroke patients present passive stiffness, that contributes to total plantarflexor stiffness (on the affected side), and also contributes to plantarflexor moment, leading probably to an adaptation to compensate the lack of active plantarflexor moment production [Lamontagne et al., 2000, Ribeiro, 2018]. Similar adaptations have been described in children with CP [Lorentzen et al., 2019].

In these studies, we aimed to set bases for future rehabilitation strategies using the rehabilitation robotic tool, by designing two novel control strategies: After Effects (AE) and Ground Reaction Force (GRF). In broad terms, AE consists on applying a torque downwards during swing phase; whereas in GRF, we applied a torque upwards with the shape of ground reaction force [Winter, 1991] during stance phase, in order to mimic the interaction with the floor during overground walking.

Our hypotheses were twofold: for AE, as we are applying a resistance to dorsiflexion during swing [Lam et al., 2006, Noble and Prentice, 2006]:

1. we expected an enhanced TA muscle activation when the torque was applied, *i.e.*, during swing;
2. we speculated that TA activation would decrease when the torque was removed (no longer applied, no need to compensate the torque anymore); and
3. we expected an enhanced dorsiflexion during swing after removing the torque in the short-term;

whereas for GRF, we expected an enhanced gastrocnemius medialis (GM) activation during the application of the torque, *i.e.*, during stance phase, similar to that in overground walking [Winter, 1991].

3.1 Materials and Methods

3.1.1 Participants

Ten healthy volunteers (five females and five males; age: 26.10 $\pm$ 3.81 years; height: 171.30 $\pm$ 9.75 centimetres), with no neurological injuries volunteered to participate in this study. Participants were informed about the procedures and possible discomfort associated with the experiments. After that, they gave their informed consent to participate. All procedures were conducted in accordance with the Declaration of Helsinki and approved by a local ethical committee.

3.1.2 Experimental platform

For this study, we used the ankle robot I described in chapter 2, section 2.2, page 51, with the subjects standing up, the angle of the orthosis modified as in Figure 3.1. Footedness preference for each subject was established via the Waterloo footedness test [Elias et al., 1998]. The robot was torque controlled to apply the torque profiles for the paradigms further explained in section 3.1.4.

3.1.3 Experimental protocol and data collection

For each participant, the training consisted on one session involving both exercise paradigms (randomized order - first GRF and then AE, and vice versa - to avoid the effect of the order of training) consisting on 86 steps. The full session (depicted in Figure

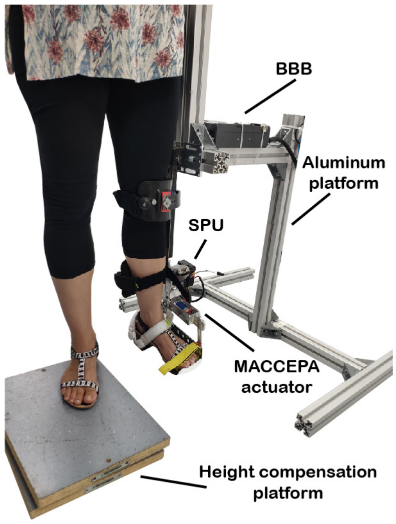


FIGURE 3.1: Volunteer attached to the robot, consisting of the MACCEPA actuator joined to the aluminum platform. The volunteer has the contralateral foot on a platform to compensation the difference of height between feet due to the robotic platform. BBB and SPU stand for Beaglebone Black and Secondary Processing Unit, and are the high level control and communications board, and low level control board, respectively.

3.2) also involved three treadmill trials (one-minute each one) at the beginning, between paradigms, and end of the session, so the overall session schema was: 1) one-minute treadmill trial; 2) GRF or AE paradigm, for three minutes; 3) one-minute treadmill trial; 4) AE or GRF paradigm, for three minutes; and 5) last one-minute treadmill trial. During the treadmill trials, participants were asked to maintain a constant walking cadence, set by an auditory metronome [Barroso et al., 2013], of approximately 0.5 steps per second.

During the two different exercise paradigms (AE and GRF), the user had to follow, via dorsi-plantarflexion, the up-downwards movement presented on the screen via a dotted line, mimicking the natural gait pattern in the sagittal plane for a healthy individual (according to Winter [Winter, 1991]) for a cadence of approximately 0.5 steps per second. The visual paradigm was implemented in Simulink, with an S-Function in charge of the video game, and Simulink blocks for UDP communications and data storage. The video game consists of a character (ball) and a line to be followed by the subject (see blue lines in Figure 3.3), while the robot exerts a controlled torque.

The user was placed on a height compensation platform (to leave free range of motion for the instrumented ankle). We placed the dominant leg of the user inside the cuffs of the grounded exoskeleton, and attached them to: the foot tip, the bridge, the heel, the shin, and just below the knee (see Figure 3.1).

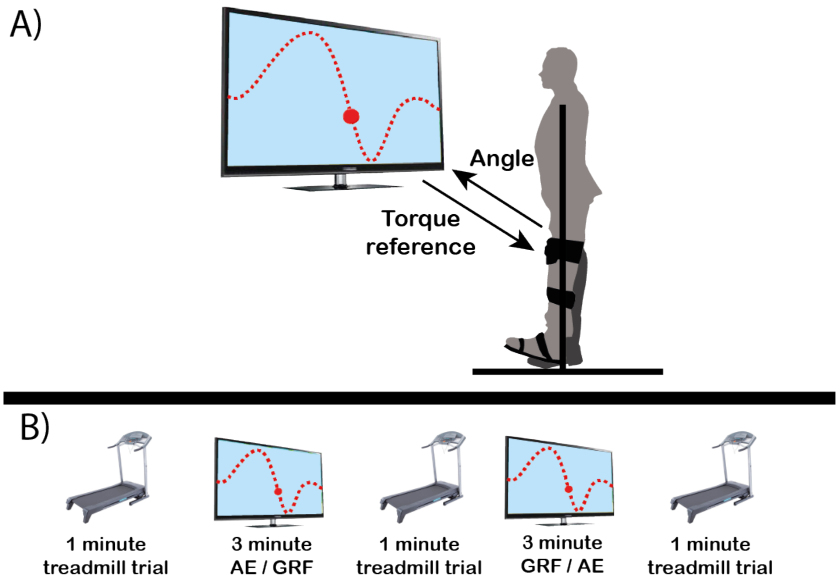
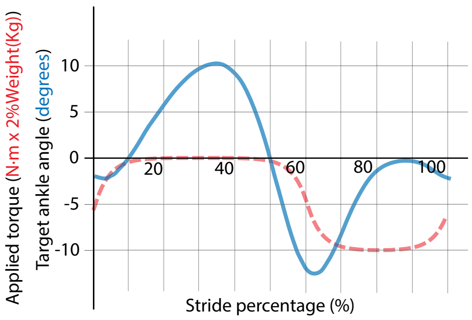


FIGURE 3.2: Experiment structure schematics. A) Upper panel shows the experimental setup. B) Lower panel shows the intervention structure: 1) one-minute treadmill trial; 2) GRF or AE paradigm, for three minutes; 3) one-minute treadmill trial; 4) AE or GRF paradigm, for three minutes; and 5) last one-minute treadmill trial.

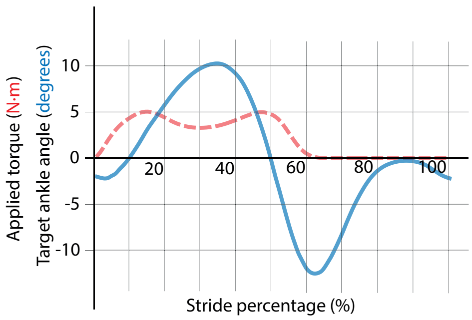
3.1.4 Exercise paradigms

Each participant executed the two different exercise paradigms (AE and GRF), as well as the three treadmill trials.

- AE: for the first 70 steps, during swing (60 to 100 % of cycle duration phase), a torque proportional to the weight of the subject (20 % of subject's weight, see dotted red line in Figure 3.3(a)) was applied downwards to force the subject to produce an enhanced dorsiflexion (and thus activate TA) to try and reach the



(a) Torque profile and trajectory to follow for AE paradigm. Torque is 20 % the weight of the subject.



(b) Torque profile and trajectory to follow for GRF paradigm.

FIGURE 3.3: Torque profiles and trajectory to follow.

prescribed trajectory. At the 70th step the force was removed, in order to observe the effect of the AE paradigm for 16 more cycles (from the total of 86 cycles).

- GRF: for the full session, during stance (0 to 60 % of cycle duration), a torque with the shape of GRF [Winter, 1991], see dotted red line in Figure 3.3, with a maximum of 5 N·m (as a technical limitation of the robot) was applied to mimic the force exerted by the floor during stance, with the aim of enhancing plantarflexion, similar to what happens in overground walking.

For the full session (five different trials), an EMG amplifier (Quattrocento, OT Bioelettronica, Torino, Italy) was used to record muscle activity of two muscles that act at the dominant ankle joint: tibialis anterior and gastrocnemius medialis. The EMG signals were recorded with an acquisition frequency of 5,120 Hz, overall gain of 150 and electronically band-pass filtered (10 - 4,400 Hz).

All SENIAM recommendations [Hermens et al., 1999] for surface EMG (sEMG) recording (shaving the area where the electrodes would be placed and cleaning the skin with alcohol) and muscle identification were followed. After that, sEMG bipolar electrodes (Ag-AgCl, Ambu Neuroline 720, Ambu, Ballerup, Denmark) were placed at a 2 centimetres inter-electrode distance over the belly of the two muscles under analysis. After that, electrodes and cables were wrapped with bandages. Preliminary tests to check the quality of the signal and proper electrode positioning were also performed. A wet wristband was used as reference.

During the AE and GRF exercise paradigms, we also recorded the target and the performed trajectory with an acquisition frequency of 128 Hz.

For the treadmill trials, a foot-switch (FSR 406 - 38 x 83 mm - square, Interlink Electronics, Camarillo, CA, USA) was placed beneath the heel of the dominant leg in order to record heel strike moment during walking, as performed in [Barroso et al., 2014]. Data from the foot-switch were used to define the beginning and end of each locomotion stride.

EMG data and ankle angular position were synchronized using a common trigger signal. This synchronization signal was triggered by the volunteer with a button, to start each of the robot trials.

Data were stored and analyzed offline with MATLAB R2016a (Mathworks, Natick, MA) and IBM SPSS Statistics 20 software (IBM).

3.1.5 Data processing

3.1.5.1 EMG Analysis

Raw EMG signals were band-pass filtered offline to remove DC offset and motion artifacts [Barroso et al., 2014] (20–450 Hz, 3rd order Butterworth), demeaned, rectified, and low-pass filtered at 4 Hz (3rd order Butterworth digital), resulting in the EMG envelopes.

Based on cycle segmentation information (from foot-switch and from the robot), EMG envelopes were then resampled at each 1 % of the locomotion stride.

In order to assess TA and GM activity across trials, for each subject, we divided the analysis of EMG data into the two main gait cycle phase: stance and swing. This was done assuming that stance corresponded to 0 to 60 % of cycle duration and swing to 60 to 100 % of cycle duration. We then integrated the activity during each phase and trial, which allowed us to compare muscle activity across trials. For each participant, muscle and phase, integrated activity was normalized with the mean obtained during the first treadmill trial, which was used as baseline recording.

3.1.5.2 Kinematics

The mean trajectory performed by each participant during AE training was used to calculate the peak angle of dorsiflexion during swing.

Differences between mean trajectory during AE training and the trajectories obtained during the three phases of AE training (first 70 cycles - AE ON, cycles 1-6 after removing the torque - AE OFF 1, and cycles 7-16 after removing the torque - AE OFF 2) were assessed with rmax coefficient [Hug et al., 2011], which corresponds to the maximum of the cross-correlation between two signals, using the MATLAB xcorr function for centred data, with option = “coeff”, and the values at the output as the maximum of the xcorr function. These values give an indication of the similarity of shape of the trajectories.

For each participant, differences between maximum target angle and maximum performed angle during AE training were calculated.

3.1.6 Statistical analysis

After applying the Shapiro-Wilk test, data showed variables with normal distributions and variables without normal distributions. Thus, together with the size of the sample (N=10), I provide the results for non-parametric tests.

The changes in the EMG for both conditions were assessed with Friedman tests of differences among repeated measures, evaluating the size effect with Average Spearman rho ($\overline{\rho_s}$).

Finally, to compare the different performed angular positions (before and after removing the torque) for the AE condition and the target angular trajectory, I used the Wilcoxon signed-rank test, evaluating the size effect by Cliff's δ test.

3.2 Results

In this section, I provide for both paradigms the results, preceded by the descriptive statistics of the involved metrics.

3.2.1 After Effects paradigm

Table 3.1 provides the descriptive statistics for the EMG in AE paradigm.

TABLE 3.1: Descriptive statistics for the EMG under AE paradigm, normalized to the mean of Treadmill 1 trial. AE ON stands for the first 70 cycles with the torque application on; and AE OFF 1 and 2 for, for the cycles 1-6 and 7-16, with the torque no longer applied, respectively.

			mean	median	standard deviation	min	max
Stance	TA	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		AE ON	2.89	2.40	2.27	0.94	8.82
		AE OFF 1	2.12	1.84	1.29	0.65	4.74
		AE OFF 2	1.87	1.75	1.15	0.49	3.97
		Treadmill 3	0.98	0.97	0.22	0.69	1.44
	GM	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		AE ON	0.31	0.30	0.17	0.10	0.60
		AE OFF 1	0.27	0.25	0.18	0.06	0.63
		AE OFF 2	0.26	0.23	0.15	0.06	0.57
		Treadmill 3	0.91	0.87	0.16	0.67	1.22
Swing	TA	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		AE ON	2.05	2.01	0.71	1.03	3.27
		AE OFF 1	1.34	1.35	0.52	0.45	2.43
		AE OFF 2	1.30	1.28	0.53	0.40	2.25
		Treadmill 3	1.05	1.02	0.18	0.84	1.48
	GM	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		AE ON	2.02	1.58	1.40	0.10	4.7
		AE OFF 1	2.05	1.54	1.93	0.13	5.77
		AE OFF 2	2.03	1.45	1.75	0.16	5.54
		Treadmill 3	1.20	1.17	0.34	0.78	1.95

Data corresponding to the different phases of the session for TA and GM muscles are represented in Figure 3.4: first 70 cycles (AE ON), 1-6 cycles after removing the torque (AE OFF 1) and 7-16 cycles after removing the torque (AE OFF 2). To test our hypotheses regarding AE training, we computed the integrated EMG activity during stance (0 to 60 % of cycle duration) and swing (60 to 100 % of cycle duration), for TA and GM. The figure represents mean integrated activity of GM and TA during AE training.

The results for the Friedman test for TA rendered significant differences both for stance ($\chi^2 = 21.84$; $p < 0.05$; $\overline{\rho_s} = 0.50$) and swing ($\chi^2 = 18.64$; $p < 0.05$; $\overline{\rho_s} = 0.41$); whereas for GM, they were only significant for stance phase ($\chi^2 = 30.64$; $p < 0.05$; $\overline{\rho_s} = 0.74$). For all conditions, EMG activity was similar when comparing baseline and Treadmill 3 (after AE training).

1. TA activity increased during swing in AE ON session when compared to baseline (Treadmill 1), which confirms our first hypothesis, enhanced TA activation during swing when AE torque is applied (see Figure 3.4 C, right panel).

2. Integrated activity of TA during swing decreased when the torque was removed (see Figure 3.4 C, swing phase, AE ON vs. AE OFF 1) which confirms our second hypothesis. Integrated activity of TA during swing was similar for the 1-6 cycles and the 7-16 cycles when the torque was no longer applied, which indicates that subjects return to baseline activity relatively fast. GM during swing does not present significant changes (although reaches a mean value of twice the activation on the treadmill), but presents high deviation, showing high variability between trials.

3. We expected an enhanced dorsiflexion during swing after removing the AE torque.

   This was also confirmed (see Figure 3.5). Table 3.2 provide the descriptive statistics for the kinematic data analyzed in AE paradigm. Subjects learned to adjust to the trajectory while the torque was on (AE ON), as the Wilcoxon test between target trajectory and AE ON condition rendered non significant differences. When the torque was removed, we found significant differences in the Wilcoxon test between target trajectory, median -3.35, and both AE OFF 1, median 3.75 ($Z = -2.80$; $p < 0.05$; Cliff's $\delta = -1$) and AE OFF 2, median 0.94 ($Z = -2.80$; $p < 0.05$; Cliff's $\delta = -1$), indicating that the users were not able to follow the target trajectory right after removing the torque. Nonetheless, in Figure 3.5 A, there is a trend of the AE OFF conditions to the target, indicating that users tend to recover when the torque is no longer applied. Furthermore, the cross correlations depicted in the figure show a high correlation, but with a lag that go from around 1 % with the torque on (AE ON), to around 4 % in AE OFF 1 and down to around 2.5 % for AE OFF 2. These also indicates that users tend to recover after removing the torque. Besides, it also indicates that, when the torque is removed, the trend is to anticipate the dorsiflexion, probably as part of the strategy to adapt to achieve the target trajectory when the torque was on.

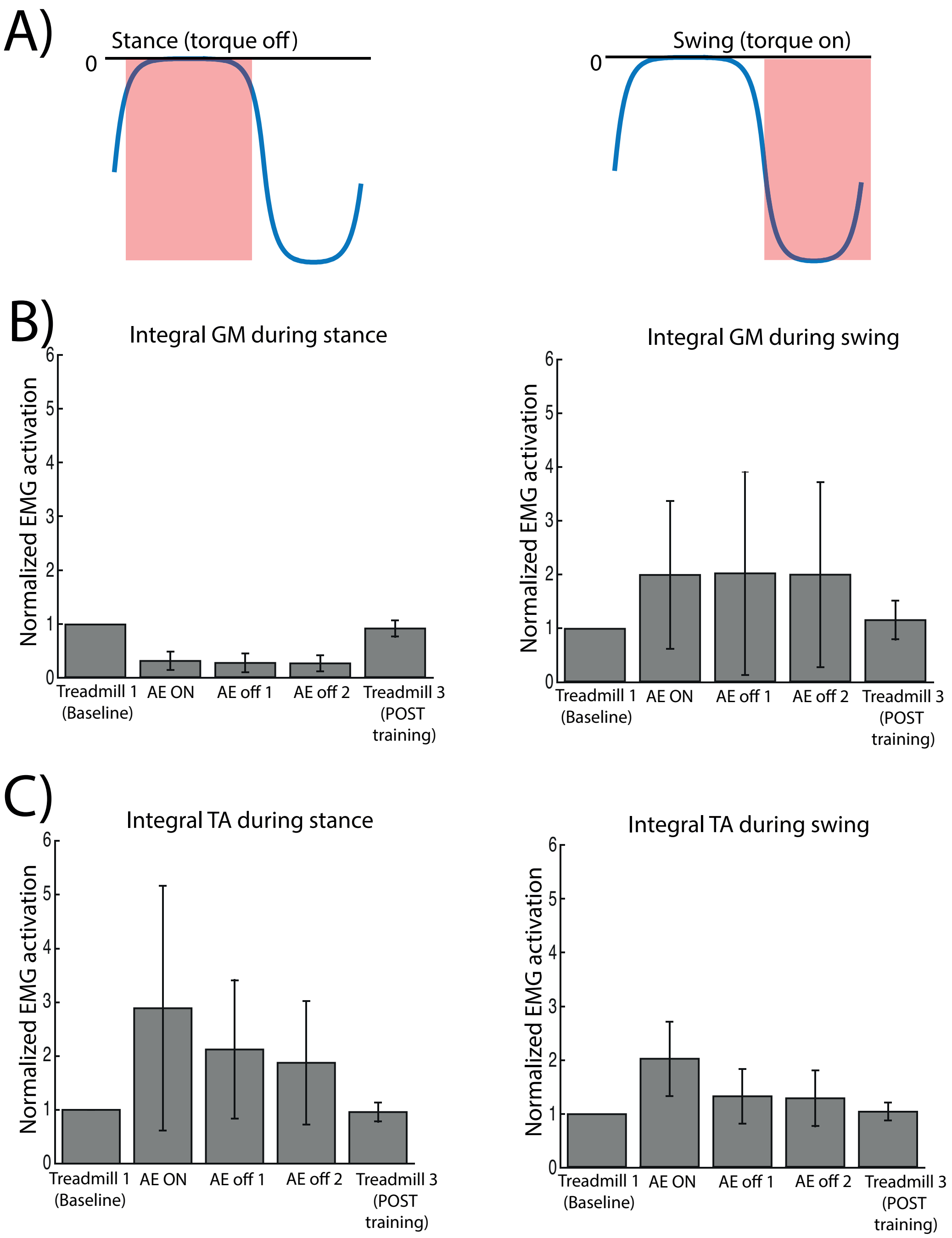


Figure 3.4: A) Representation of the torque profile delivered during stance and swing during AE. B) Integral of GM activation during stance (left panel) and swing (right panel), normalized to the baseline, *i.e.* Treadmill 1. C) Integral of TA activation during stance (left panel) and swing (right panel), normalized to the baseline, *i.e.* Treadmill 1, mean and standard deviation. B and C are given for Treadmill 1 (baseline), first 70 training cycles with the torque (AE ON), first 1-6 training cycles without the torque (AE OFF 1), last 7-16 training cycles without the torque (AE OFF 2), and Treadmill 3 (after training).

Table 3.2: Descriptive statistics for the EMG under AE paradigm.

	mean	median	standard deviation	min	max
Target trajectory	-3.35	-3.35	0.00	-3.35	-3.35
AE ON	-3.25	-2.80	1.82	-6.58	-0.72
AE OFF 1	3.58	3.75	1.97	-0.46	6.35
AE OFF 2	1.24	0.94	1.66	-2.02	4.11

3.2.2 Ground reaction force (GRF) paradigm

Table 3.3 provides the descriptive statistics for the EMG in GRF paradigm.

We hypothesized an enhanced GM activation during the application of the torque (stance). Interestingly, this hypothesis was not verified (see Figure 3.6 B, left panel). Integrated activity of GM during stance was significantly ($\chi^2 = 15.80$; $p < 0.05$; $\overline{\rho_s} = 0.77$) lower during GRF training than during baseline (Treadmill 1). The rest of muscles and phases rendered non-significant changes in the Friedman tests, *i.e.*, the task did not elicit any significant changes on TA activation on the full gait cycle, nor in GM during swing.

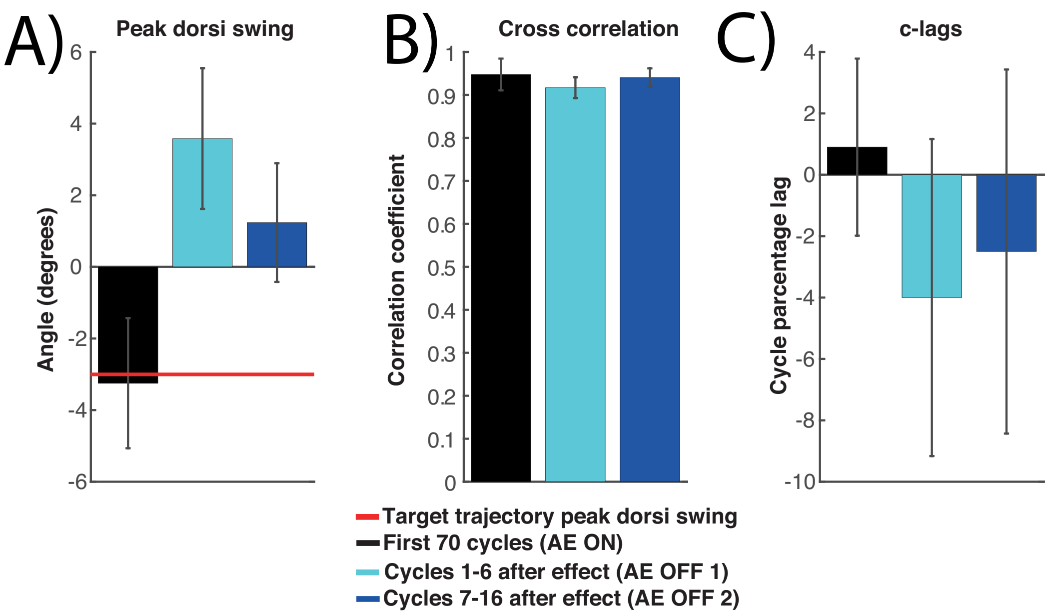


Figure 3.5: A) Angular peak for dorsiflexion during swing. B) Cross correlation coefficients of ankle angle for the three AE conditions (AE ON, AE OFF1 and AE OFF 2) with the target trajectory, regardless of phase delays. C) Cross correlation lag between the three AE conditions and target trajectory, unit in percentage of cycle. Negative lag means that the waveform happened earlier.

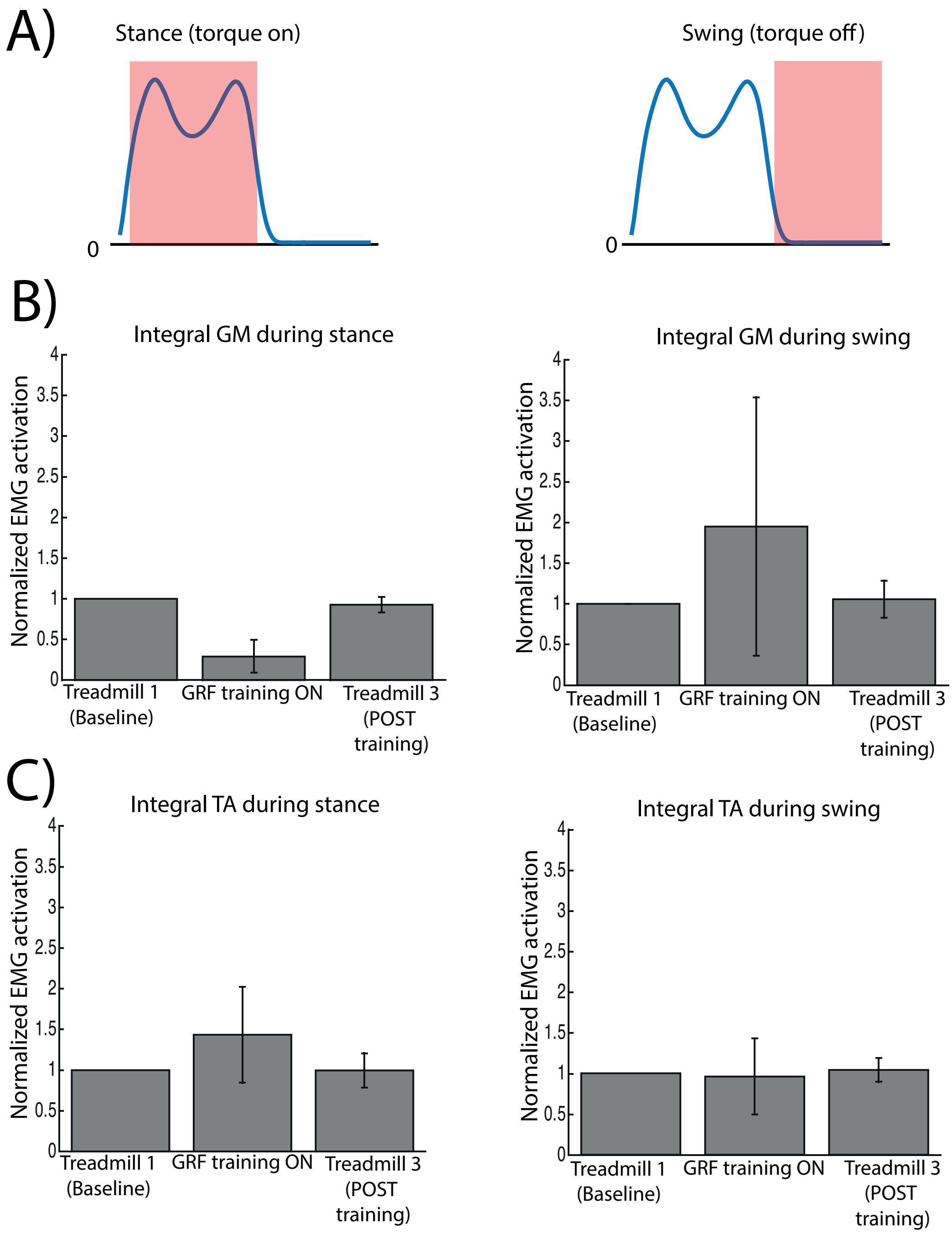


FIGURE 3.6: A) Representation of the torque profile delivered during stance and swing under GRF paradigm. B) Integral of GM activation during stance (left panel) and swing (right panel), normalized to the baseline, *i.e.* Treadmill 1. C) Integral of TA activation during stance (left panel) and swing (right panel), normalized to the baseline, *i.e.* Treadmill 1, mean and standard deviation. B and C are given for Treadmill 1 (baseline), training cycles with the torque applied (GRF), and Treadmill 2 (after training).

TABLE 3.3: Descriptive statistics for the EMG under GRF paradigm.

			mean	median	standard deviation	min	max
Stance	TA	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		GRF	1.44	1.42	0.59	0.65	2.39
		Treadmill 2	0.98	0.96	0.17	0.65	0.28
	GM	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		GRF	0.29	0.22	0.20	0.09	0.63
		Treadmill 2	0.95	0.93	0.08	0.84	1.06
Swing	TA	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		GRF	0.96	0.79	0.47	0.43	1.77
		Treadmill 2	1.04	1.00	0.13	0.86	1.33
	GM	Treadmill 1	1.00	1.00	0.00	1.00	1.00
		GRF	1.95	1.55	1.59	0.25	4.92
		Treadmill 2	1.02	0.98	0.25	0.77	1.60

3.3 Discussion

Motor learning of new gait patterns during treadmill walking seems to be more dependent on the amount of practice than the difficulty and variations of task practice [Krishnan et al., 2019].

This approach can eventually be used to rehabilitate walking and, eventually, may target spasticity. As a consequence of spasticity, the quality of walking function in neural-impaired patients is affected [Krawetz and Nance, 1996]. More than 60 % of SCI patients develop spasticity symptoms [Tazoe and Perez, 2015], mainly associated with flexor/extensor spasms triggered by cutaneous stimulation [Bennett, 2008]. In stroke, about 27 % of patients suffer from spasticity. This percentage increases up to 43 % on the brink of chronicity (at 6 months after the lesion), and down to around 34 % in chronic patients (after 18 months) [Kuo and Hu, 2018]. Recently, Stampacchia et al. [Stampacchia et al., 2016] have reported a decrease in muscle spasticity in SCI patients that participated in a walking session assisted by an exoskeleton. Morone et al. [Morone et al., 2017] recently stated that although studies have found that intensive training short after stroke can lead to spasticity increases [Krakauer et al., 2012], robotic therapy could help decrease the risk of spasticity on anti-gravitational muscles, as it allows an early verticalization with reduced effort.

Our results showed that, for AE paradigm, our expectations of enhanced TA activation during swing with the torque on, and decreased activation when the torque was removed, were confirmed (medium effect size -according to Koltrlik and Williams [Kotrlik and Williams, 2003]). Furthermore, the increased dorsiflexion after removing the torque was also confirmed (large size effect -according to Romano et al. [Romano et al., 2006]-). No significant changes were found when comparing Treadmill 1, Treadmill 3 and AE OFF 2, for stance and swing in TA, and swing in GM, indicating that the activation is not significantly different for that in overground walking when the torque is removed.

On the GRF paradigm, although there were no changes in the muscles and phases we were not focusing at, *i.e.* TA, and swing for GM; our hypotheses of GM enhanced activation in stance were not confirmed. This result can be related to the low amplitude of the torque applied to the user when mimicking the stance phase in comparison to that of natural overground gait (5 N·m vs. slightly more than 100 % weight of the subject), rendering our treatment similar to a body weight supported gait. BWS have been reported to attenuate GM activation, as the antigravity function is less demanded under such condition [Ivanenko et al., 2002]. Van Kammen et al. [Van Kammen et al., 2014] also reported the effects of BWS on decreased stance GM activation, pointing to modifications on the sensory cue that drives ankle flexo-extension. Furthermore, these authors also found that TA tend to increase the activation when wearing an exoskeleton, probably due to the interaction between human and robot, and although this increased activation tends to diminish when the BWS rises, it also tends to increase when the speed decreases. These findings are consistent with ours, where although non-significant, we have provided increased TA activation in stance, even when no torque was applied.

Apart from the reduced GM activation in stance, the fact that when there are no effects in GM swing, and both for swing and stance, leads us to conclude that the use of the robot is not negatively influencing the natural motor activation sequence.

Chapter 4

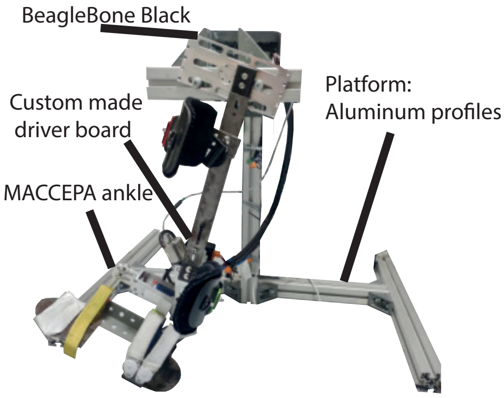
Development of the platform

In this chapter I present the final development of the rehabilitation robotic tool, with its mechanical structure and TAd applied to a torque controller. I expose the design, development (both in section 4.1), and tests (in section 4.2), of the video game used as the visual feedback for the rehabilitation task, in the framework of the description of the full system. The use of a video game is framed not only in the need to provide the subject with feedback, but the requirement for it to be engaging and challenging, to promote adherence to the task, and potentially enhancing the outcome. Afterwards, I describe the controller that includes our proposed haptic adaptive feedback approach (HAF, in section 4.3), based on tacit adaptability paradigm. I finally present the first tests with healthy subjects [Asín-Prieto et al., 2017c] in section 4.4 (tests are further extended in chapter 5, page 97).

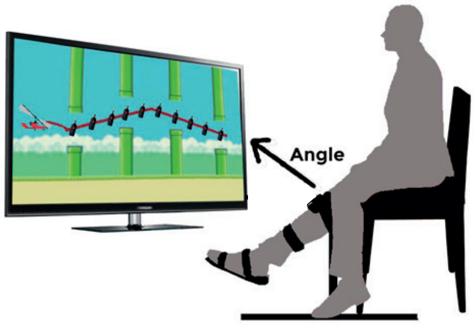
4.1 Description of the final rehabilitation tool

The system consists of several components, depicted in Figure 4.1(a): 1) a platform based MACCEPA ankle, 2) power and low level control electronics embedded in the actuator: SPU, 3) higher level electronics for communication and high level control purposes, implemented into a BBB, and 4) visual paradigm.

1. For the platform based MACCEPA ankle actuator (see Figure 4.2(a)), we built in the laboratory a platform made of commercially available aluminum profiles. This platform, in the attachment to the MACCEPA ankle module permits the adjustment of the angle of the knee, for a comfortable position for the user, or for different therapies, as the presented in chapter 3, page 71. This MACCEPA ankle actuator has the footplate modified for easier torque production by the wearer: we connected both parts to form a whole one-piece footplate (as opposed to the two



(a) Mechanical structure and robot.



(b) Full platform schema.

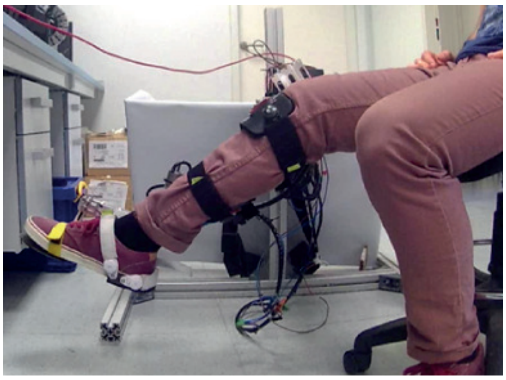
FIGURE 4.1: Complete platform.

separate footplate parts seen in Figure 2.7 (in chapter 2, section 2.2.1, page 51), as seen on the actuator detail in Figure 4.2(b).

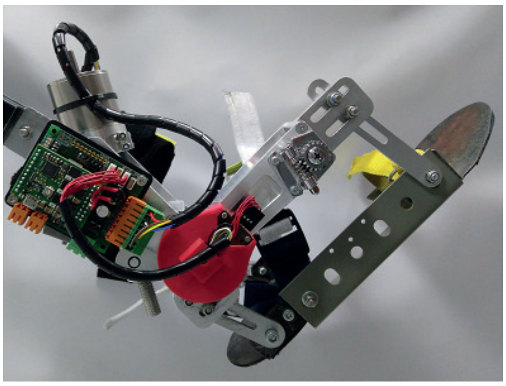
2. This item is the SPU (refer to chapter 2, section 2.2.2, page 54, for description), in which I implemented the TAd controller (see section 4.3).

3. The BBB (explained in chapter 2, section 2.2.2, page 54) runs a custom-made program that provides the framework for the communications between the visual paradigm and the low level control electronics. This program reads the angular position sent by the actuator via the SPU and sends it to the visual paradigm to control the character on the screen. The visual paradigm sends its status to the BBB, and the BBB sends the torque reference to the SPU, closing the synchronization between the visual paradigm and the robotic platform.

4. The visual paradigm is implemented in Simulink, with an S-Function in charge of the video game, and Simulink blocks for UDP communications and data storage. The video game has been developed to maintain the computational cost as low



(a) Subject inside the robotic platform.



(b) MACCEPA actuator detail.

FIGURE 4.2: Proposed robotic platform.

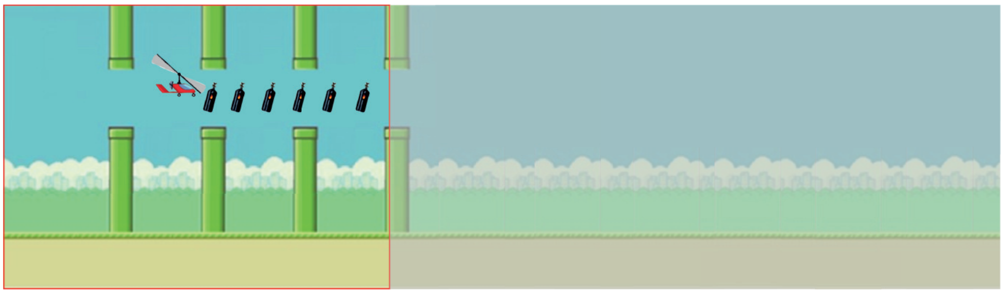
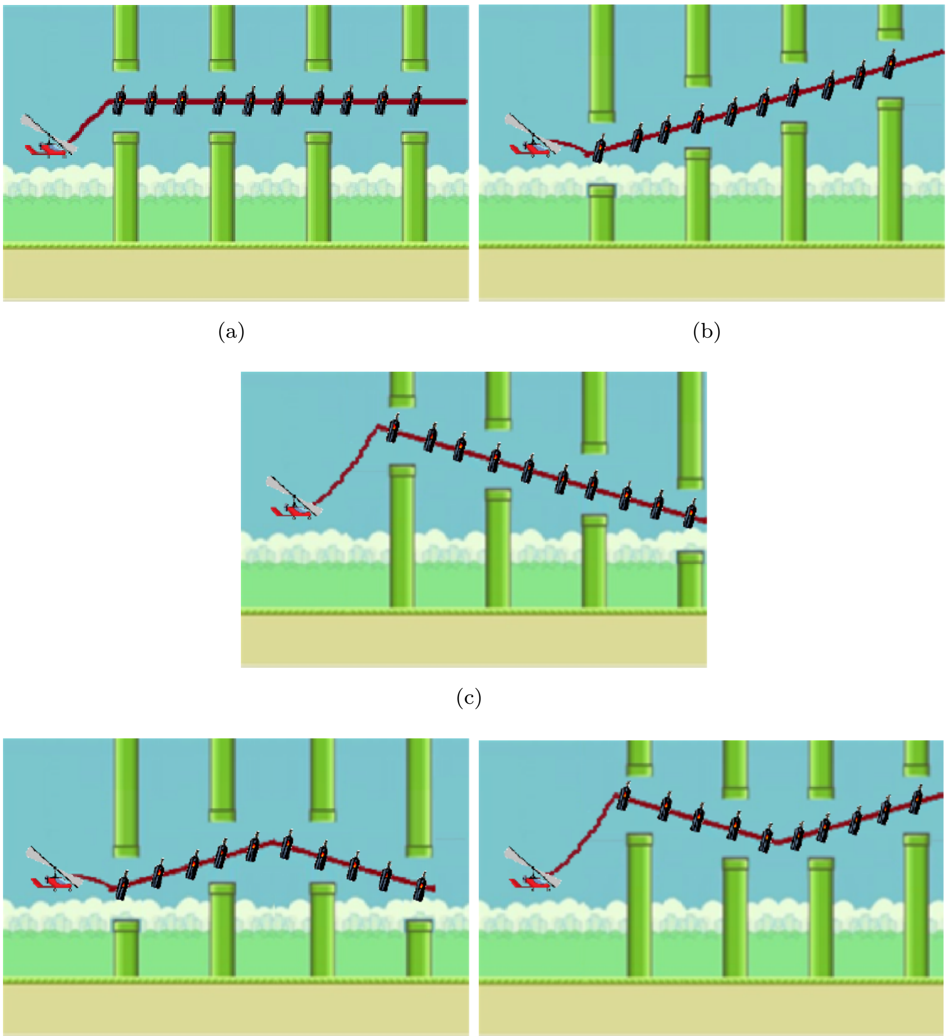


FIGURE 4.3: Visual paradigm. Visible section (left) contains the only items that are generated; greyed section (right) is not onscreen, and thus its items are not generated to save memory and computational cost.

as possible by means of generating only the items visible on the screen and not the whole "world" (as shown on Figure 4.3). The visual paradigm consists of a sequence of collectible onscreen items (gas bottles), and a character (gyrocopter) that can be moved with the angular position of the ankle via dorsi-plantarflexion. There are five possible trajectory profiles to be followed (depicted in Figure 4.4, the resting position of the ankle was set in -2.5 degrees, as the most comfortable position for the users).

The task instruction was to follow the trajectories delineated by means of the sequence of gas bottles, regardless of any perturbation made by the robot (these perturbations are task and therapy dependent, and thus, customized for each application). The user had to move the gyrocopter with the angular position of the ankle via dorsi-plantarflexion: dorsiflexion implies moving the avatar upwards in the screen, whereas plantarflexion implies going downwards. Meanwhile, the robot disturbed the user motion by performing plantar and dorsiflex alternated torque profiles (see Figure 4.5), with the aim of stimulating both agonist and antagonist muscle groups, both in dorsi and plantarflexion movements. These alternated dosri-plantarflexion torque paradigm was developed with the aim of stimulating both agonist and antagonist muscle groups.

We established two different metrics to immediately quantify the performance of the user: Score and root mean squared error (RMSE). The first one, **Score**, is calculated instantaneously per trial by comparing the number of collected and total (collected + uncollected) onscreen items; whereas **RMSE** is calculated by performing the root mean square over the subtraction of the performed trajectory and the ideal linear path between onscreen items.



(a) (b) (c) (d) (e)

FIGURE 4.4: Representation of the five possible trajectory profiles: a) constant -2.5 degrees; b) straight increasing from -4 to 1 degrees; c) straight decreasing from -1 to -6 degrees; d) from -6 to -2.5 and back to -6 again; and e) from 1 to -2.5 and back to 1.

4.2 Viability study of the robotic platform

4.2.1 Introduction

In this study we focused on the evaluation of detailed strength-producing and position-control metrics and the correlation with the learning of sub-maximal force production control during a new position-maintenance task for early rehabilitation after stroke [Panjan et al., 2011]. We used for this study the final platform described in section 4.1, with a zero-torque control. We introduced disturbances during the exercise to make it more difficult, increasing the intensity of the training, and potentially inducing improved learning [Turner et al., 2013], although it is of prominent importance for this increased difficulty to not exceed subject's capabilities, otherwise little or no improvement could be

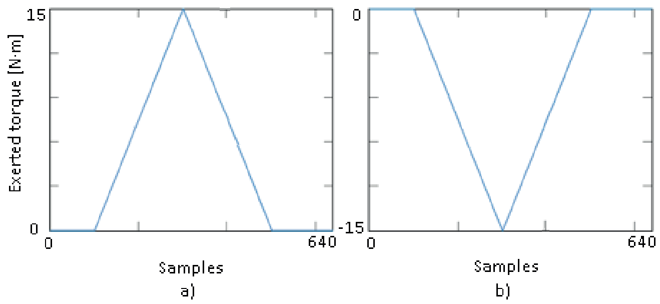


FIGURE 4.5: Possible torque profiles. a) and b) show the torque to dorsiflexion (up) and plantarflexion (down) direction, respectively.

expected [Asín-Prieto et al., 2014a]. Our hypothesis was that the ability to perform the task of high precision position-maintenance with sub-maximal force production during disturbances at the lower-limb over time could promote improvements in ankle control after stroke.

4.2.2 Materials and methods

4.2.2.1 Participants

Nine males and six females without any history of neuromuscular and cardiovascular disorders participated in this study; with ages 27.73 ± 3.58, and sport activity more than two and less than six hours per week.

4.2.2.2 Task description

The experiment consisted on following the trajectories depicted via the visual paradigm, while the robot disturbed the user motion by performing plantar and dorsiflex alternated torque profiles (already explained in section 4.1). The aim of the exercise was to improve the motor control by learning how to maintain the position to follow the trajectory in the screen, compensating the perturbations done by the robot.

The task consisted on forty trajectories, distributed as in Figure 4.6: 1) the first trajectory allowed the user move the foot freely to understand the dynamics of the exercise; 2) the three trials from 2 to 4 assessed the performance of the subject in the task before the training (at fixed torque, established at 15 N·m as a technical limitation of the robot-controller set); 3) thirty training trajectories were performed (one of the three possible training paradigms, explained in section 4.2.2.3, was randomly selected for each user); 4) the three trials from 35 to 37 assessed the performance of the subject in the task after the training, at 80 % of the fixed torque, *i.e.* 12 N·m (in order to assess the performance at a different level than that used for training in the fixed torque training

FIGURE 4.6: Experiment phases.

paradigm); and 5) finally, the last three trials from 38 to 40 assessed the performance of the subject in the task after the training.

4.2.2.3 Training paradigms

Three training paradigms were designed for the experiment:

- Fixed torque: This training paradigm performed the thirty trajectories at a fixed torque (15 N·m).
- Progressive: This paradigm progressively increased the torque exerted by the robot from a minimum of 1 N·m up to 15 N·m.
- Modulated: The peak torque exerted in each trajectory was increased in 2 N·m if score in the previous one was 100 %, and decreased to the average between the two last trajectories' score (saturated in this way: decreased at least 1 N·m and at most 2 N·m in comparison to previous torque). For example, if score was lower than 100 %, previous peak torque was 8 N·m, and current torque was 10 N·m, then next torque would be $(8 + 10)/2 = 9$ N·m, due to the difference $10 - 9 = 1$ N·m being higher or equal to 1 and lower or equal to 2 N·m.

4.2.3 Results

Figure 4.7 depicts the scores for the three training paradigms (average and standard deviation) together with the trend (calculated as the fitting of the two fixed torque assessments). We observed that the score increased after the training, and that the score for the assessment at the 80 % of the fixed torque at the end of the training was better for all training paradigms.

Figure 4.8 shows the root mean squared error for the three training paradigms. Lower errors were obtained after the training.

In Figure 4.9 we observed that for the average interaction torque for the three training paradigms, separated in dorsi and plantarflex trials: 1) in the fixed torque training paradigm, all the subjects reached the target of 15 N·m; 2) in the progressive paradigm, this increase was logically progressive in the measured torque; and 3) in the torque modulation training paradigm, the torque increased up to a plateau, depending on each subject's score, not reaching the prescribed torque in any case.

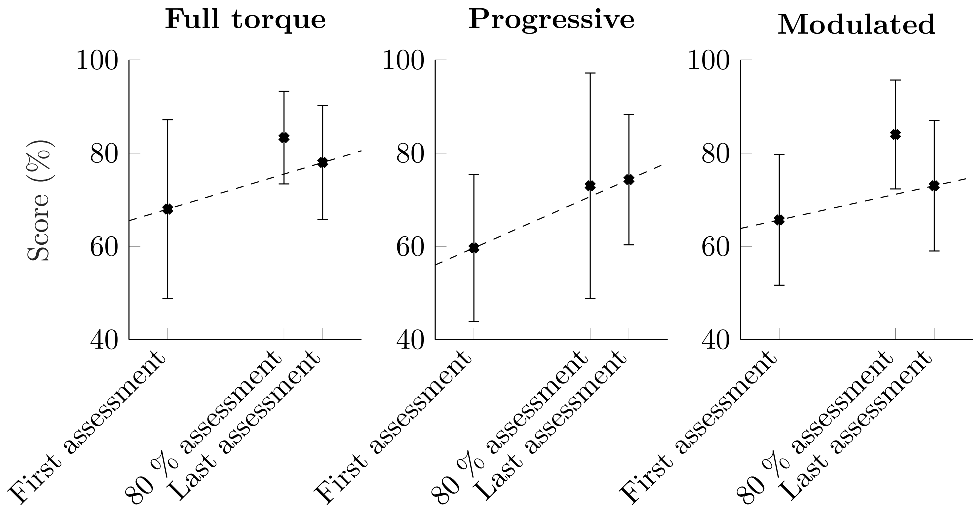


FIGURE 4.7: Scores for the three training paradigms (average and standard deviation), for the three assessments: 1) Before training at fixed torque, 2) after training at 80 % of fixed torque, and 3) after training at fixed torque.

4.2.4 Conclusions

We observed that all training paradigms led to an improvement in the score comparing pre and post-training performances, so we concluded that this platform induces learning on healthy subjects. Consistently, the error of the subject when positioning the gyrocopter on the visual cue (*i.e.* maintaining the foot at -2.5 degrees), before and after training, decreased.

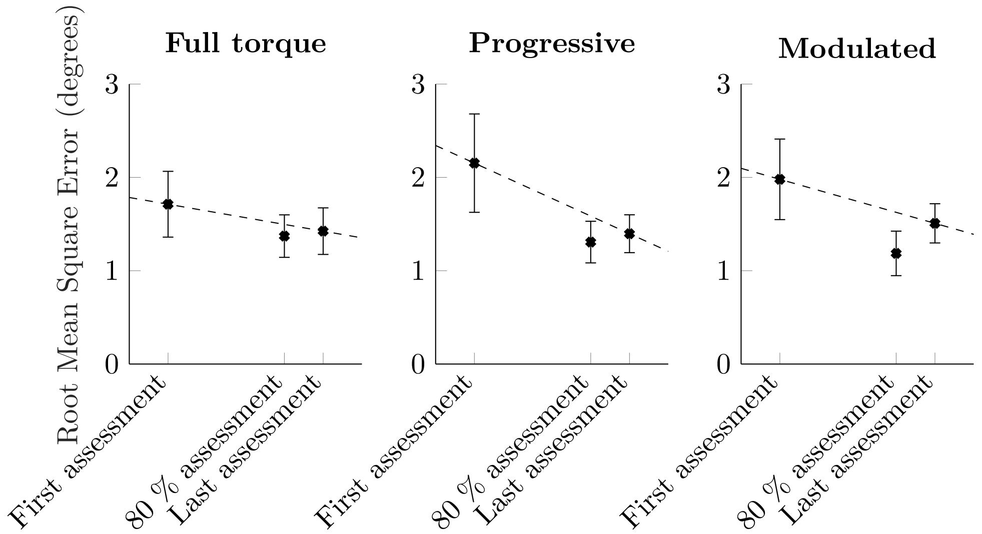


FIGURE 4.8: Root mean squared error for the three training paradigms (average and standard deviation), for the three assessments: 1) Before training at fixed torque, 2) after training at 80 % of fixed torque, and 3) after training at fixed torque.

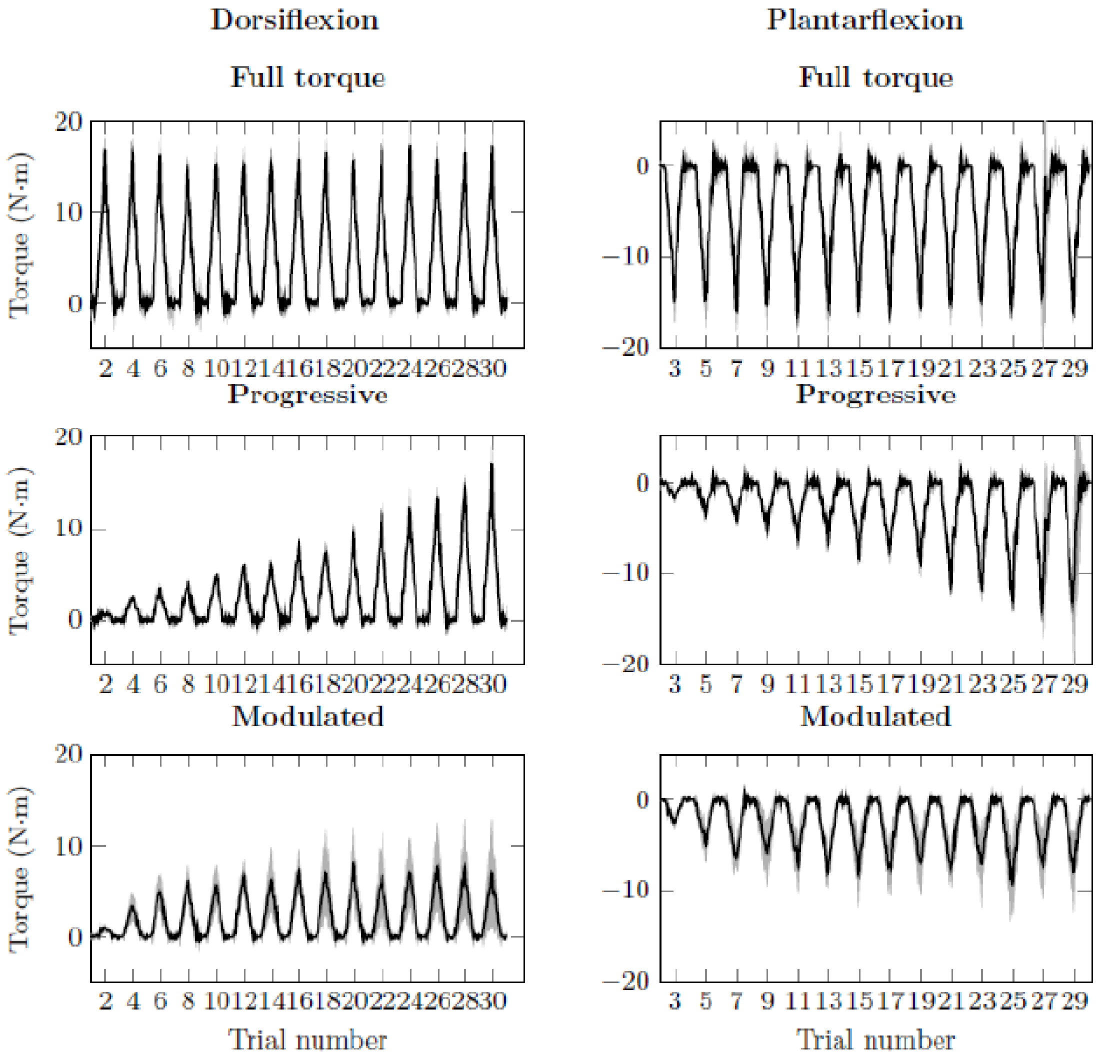


FIGURE 4.9: Torque for the three training paradigms, separated in dorsiflexion and plantarflexion. Average is represented with a solid black line, and standard deviation is represented by the grey shadow in the figure.

All the users for the cases of fixed torque and progressive torque paradigms obviously reached the prescribed torque, but this was not the case for the modulated torque paradigm, where none of the users was able to reach this 15 N·m torque during the training, so we concluded that this torque exceeded our approach of using sub-maximal force production, at least for some of the subjects.

All the subjects reported that they liked the game, and most of them said that it was too easy. This is also observable looking into the reached scores.

4.3 Final robot controller

Once we demonstrated the usability of the platform, we developed the final controller, described in the next lines.

The controller of the robotic platform presented in section 4.1 comprises a zero torque controller (based on a classic PID implementation) and the haptic adaptive feedback component, based, in turn, on tacit adaptability. The controller is described by equation 4.1.

$$u = \tau_{PID} + HAF \tag{4.1}$$

where u is the output of the controller (pulse width modulation), τ_{PID} corresponds to the torque controller (equation 4.2), and HAF to the HAF module (equation 4.3).

$$\tau_{PID} = K_p \cdot error + K_i \cdot \int_0^t error \cdot dt + K_d \cdot \frac{d}{dt} error \tag{4.2}$$

where K_p, K_i and K_d are respectively the PID constants.

$$HAF = K_{HAFi} \cdot \int_0^t \alpha \cdot dt + K_{HAFp} \cdot \alpha \tag{4.3}$$

where K_{HAFi} and K_{HAFp} are respectively the integral and proportional constants of the HAF module; α angle is proportional to the interaction torque between human and robot; and $error = LA_{ref} - LA$. LA is the actual sensor information for the Lever Arm angle, whereas LA_{ref} is the calculated reference LA angle. This reference LA angle is calculated with the approximation of the MACCEPA actuator to a torsion spring actuator described by equation 4.4.

$$LA_{ref} = \frac{\tau_{ref}}{K_{ts}} + FL \tag{4.4}$$

where τ_{ref} is the reference torque to the controller, K_{ts} is the empirically obtained torsional stiffness constant, and FL is the Fixed Link angle, *i.e.* the user's ankle angle.

The objective of the controller is to apply higher torques when higher scores are reached (consequently getting more difficulty on the task), and vice versa (rendering the task easier with lower scores). To do this, K_{HAFi} and K_{HAFp} are empirically set to $\frac{K_{HAF}}{10}$ and $\frac{K_{HAF}}{0.05}$, where K_{HAF} provides the modulation of the torque following this simple rule: $K_{HAF} = (100$ - Score [%]$)/100$.

The HAF module is schematically introduced in Figure 4.10, along with the rest of the control architecture.

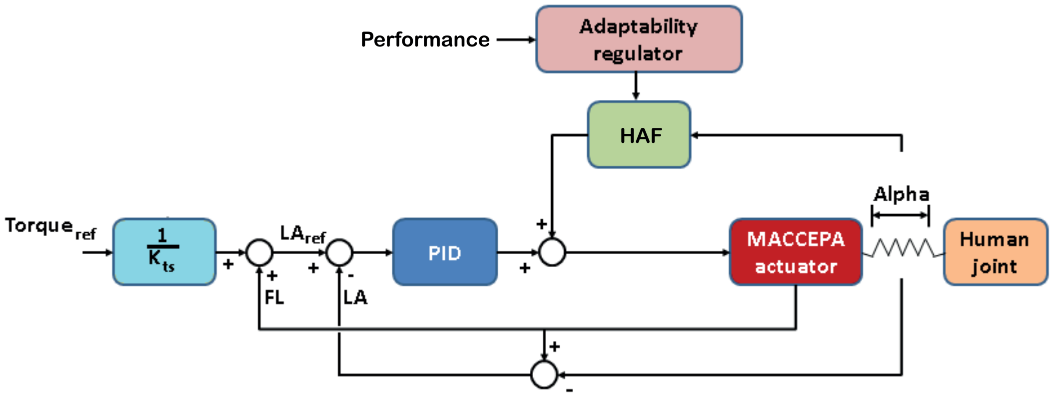


FIGURE 4.10: The controller of the robot comprises a zero torque controller (PID) and the TAd module (TAd constant -K_{TA}- multiplied by alpha, angle proportional to the interaction between the robot and the subject), tweaking K_{TA} with the performance. The subject controls the location of the character on the screen by means of the ankle joint angle.

4.4 Preliminary protocol test

This study extends the one in section 4.2. In this case, we provide a novel approach in using HAF to modulate the compliance of a torque control, to in the end modulate the difficulty of the task and thus play around the concept of the "challenge point theory"[Guadagnoli and Lee, 2004] to try accelerate the rehabilitative process. We intend to improve the therapy for stroke by training the ability of maintaining the position of the foot, addressing the typical problem for these patients of foot-drop, as we focus our actuation on dorsi/plantar-flexion.

4.4.1 Materials and Methods

In this section, I briefly present the platform we used for this study and expose the methodology.

4.4.1.1 Participant

One healthy subject, right-handed, 30 years old, was enrolled for this experiment.

4.4.1.2 Task

The task instruction was to follow the trajectories delineated in the visual paradigm by the gas bottles, moving the gyrocopter with the angular position of the ankle. Meanwhile, the robot disturbed the user motion by performing plantar and dorsiflex alternated torque profiles, modulated with HAF paradigm (see Figure 4.11). The behaviour of the

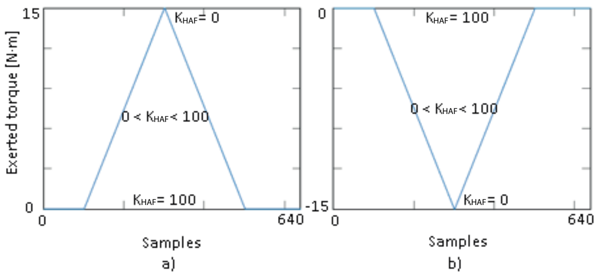


FIGURE 4.11: Modulation of the torque profiles. Torque to dorsiflexion (up) and plantarflexion (down) direction, with the behaviour of the HAF module: 1) $K_{HAF} = 1$ leads to zero-torque control; 2) $K_{HAF} = 0$ leads to regular torque control, so up to 15 N·m; and 3) K_{HAF} between 0 and 1, closer to zero-torque control the higher K_{HAF} is.

HAF module is: $K_{HAF} = 1$ leads to zero-torque control; $K_{HAF} = 0$ leads to regular torque control, so up to 15 N·m; and K_{HAF} between 0 and 1, closer to zero-torque control the higher K_{HAF} is. The aim was to improve the motor control by learning how to maintain the position to follow the trajectory in the screen, compensating the perturbations.

4.4.1.3 Longitudinal experiment structure

The task consisted in five sessions, of 61 trajectories (see Figure 4.12): 1) first trajectory to understand the dynamics of the exercise; 2) the next ten assessed the performance before the training (at fixed torque); 3) forty training trials were performed; and 4) finally, the last ten trials assessed the performance after the training.

4.4.1.4 Data Analysis

We analyzed the results by looking into the score, and the error between performed and prescribed trajectories, for ten trajectories before (PRE) and after (POST) the 40 trials training. We provide standard error for score and root mean square error (RMSE) as measurements of the variability on the performance along the assessments, meaning better motor control with higher homogeneity on the mean values, *i.e.* more similar values along the full assessment. We performed a 2-Way ANOVA of repetitive measures for the statistical analysis with assessment (PRE-POST) and session (1 to 5) factors and a Bonferroni's post-hoc analysis, with a $p = 0.05$.

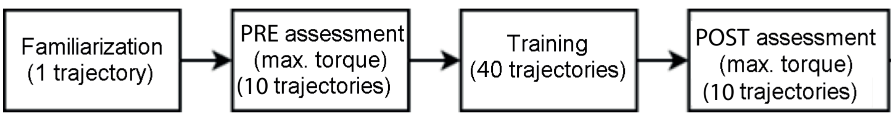


FIGURE 4.12: Experiment phases.

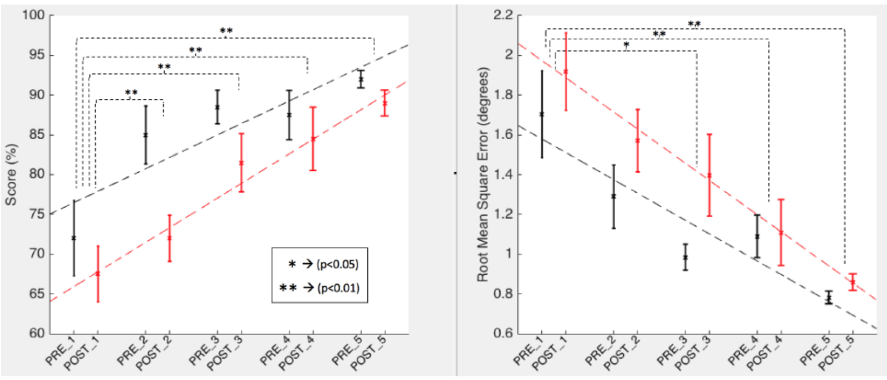


FIGURE 4.13: Scores and RMSE (average, and standard error) before (PRE) and after (POST) each training assessments. Dotted line represents the linear fitting of the data for PRE (black) and POST (red) assessments.

4.4.2 Results

In the results we observed statistical (session factor, $p < 0.05$) increment on the score ($F(4, 36) = 15.8, \eta_p^2 = 64\%$) and reduction on the RMSE ($F(4, 36) = 15.5, \eta_p^2 = 63\%$). Post-hoc analysis revealed significant changes inter-sessions, as shown in Figure 4.13. We found no intra-session significant changes.

4.4.3 Conclusions

The observed reduction in the variability together with the improvements in terms of score and reduction on error along the sessions suggests that the protocol is a successful training for motor control, and that two days were enough for the user to significantly increase the score, and three to significantly decrease the error. No significant differences were observed on standard error (increase) and score (decrease) between pre and post-training intra-session, which may suggest a potential effect of fatigue. The term haptic adaptive feedback is coined to refer to this combination of feedback paradigm and controller integrating HAF module.

4.5 Conclusions of the chapter

In this chapter, I have exposed the actual development of the final tool, with TAd applied to a torque-controlled MACCEPA ankle actuator on what we called haptic adaptive feedback, modulating TAd value with a therapy-intrinsic metric: the score on the task, being the task a video game based visual feedback where the subjects had to collect items in a scrolling screen.

To sum up, we concluded that the developed tool was useful to potentially induce learning in healthy subjects, and thus we kept improving the training paradigms (evaluation and results presented in chapter 5, page 97), for the translation into a rehabilitation tool.

Chapter 5

Evaluation of haptic adaptive feedback to promote motor learning

This chapter describes the experimental study to test the developed T1 phase centred protocol we designed. T1 rehabilitation phase is focused on the preparatory training based on joint mobilization, and thus the rehabilitation tool is used for these experiments with the patient sitting on a chair, and focus on motor control for the last stages of rehabilitation prior to going onto gait rehabilitation centred paradigms.

The objective of the study is to demonstrate the ability of the developed robotic rehabilitation tool integrated with a video game and controlled with the proposed HAF paradigm for enhancing adherence and engagement, by providing the control of the robot with the performance to modulate the task difficulty.

The hypothesis is that the use of the ankle rehabilitation robot described in chapter 4, page 84, would promote motor learning and increase corticospinal excitability of the dorsi-plantar flexor muscles. Although it is not clear the relationship between motor learning and corticospinal excitability [Bestmann and Krakauer, 2015], several authors have suggested a line between them [Naros et al., 2016, Kida et al., 2016, Perez et al., 2004, Mrachacz-Kersting et al., 2019]. Corticospinal excitability can be assessed with transcranial magnetic stimulation, via the elicitation of motor evoked potentials [Rotenberg et al., 2014]. Validation of the hypotheses provides preliminary evidence of the usefulness of this novel robotic therapy to promote motor learning in the context of a pre-gait mobilization task, *i.e.*, mobilization before undergoing gait-centred rehabilitation.

5.1 Materials and methods

5.1.1 Participants

Ten healthy subjects (29.80 ± 6.32 years old) participated in the study. They signed an informed consent for the experiment. Experiments were conducted in accordance with the declaration of Helsinki. All experimental procedures were approved by the Bioethical subcommittee of the Ethical committee of CSIC (Spanish National Research Council), reference 008/2016.

5.1.2 Experimental Platform

The ankle robot that has been cursorily described in chapter 4, section 4.1, page 84, was used in this study. Footedness preference of each subject was selected as in chapter 3, page 71. The controller of the robot has been described in chapter 4, section 4.3, page 91.

5.1.3 Protocol

The longitudinal intervention protocol applied on each participant is graphically described in Figure 5.1. The intervention lasted four days. Training sessions were performed in days 1-3. Four corticospinal assessments were performed in days 1, 3 (two assessments) and 4.

The intervention proceeds according to the following daily structure: forty training repetitions (randomized trajectory profiles, depicted in Figure 4.4, chapter 4, page 87), with torque modulated by the system; followed by ten evaluation repetitions (two types of torque profiles -in Figure 4.11, chapter 4, page 94-, multiplied by five types of trajectories) for the assessment of immediate effect. The torque provided in the evaluation repetitions was settled at the maximum given by the robot: 15 N·m. All repetitions had a duration of ten seconds per trajectory.

The task instruction was described in chapter 4, section 4.4, page 93. In summary, the aim was to follow the trajectories delineated in the visual paradigm by means of the sequence of gas bottles by dorsi/plantarflexing the ankle, to move the gyrocopter. Meanwhile, the robot disturbed the user motion by performing plantar and dorsiflex alternated torque profiles.

The subjects were asked to train and try to find a strategy to compensate for the disturbances exerted by the ankle robot, to successfully follow the trajectory on the screen, along three sessions (one every day), of 50 repetitions.

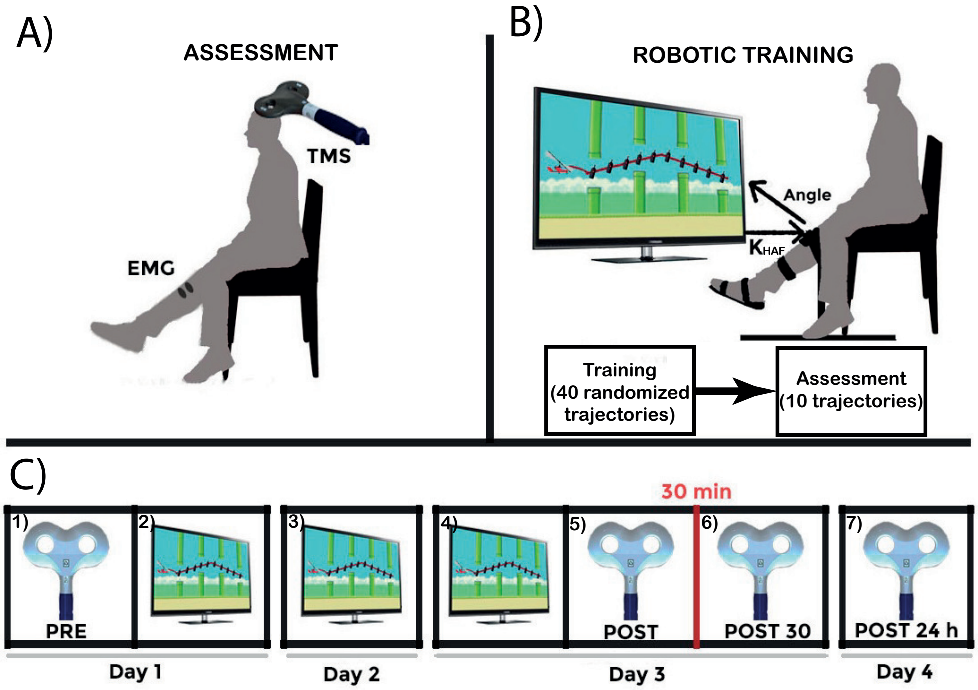


FIGURE 5.1: Experiment schematics. A) Upper left figure shows the transcranial magnetic stimulation (TMS) assessment setup. B) Upper right figure shows the experimental setup together with the daily training structure: 40 training repetitions, and ten last repetitions to survey the execution after the training (at a settled torque, the maximum given by the robot: 15 N·m). And C) Lower figure shows the longitudinal intervention structure: 1) TMS assessment (represented by the figure-of-8 coil) PRE-intervention; 2) first day training (represented by the visual paradigm); 3) second day training; 4) third day training; 5) TMS assessment POST-intervention; 6) POST30: TMS assessment 30 minutes after intervention; and 7) POST24h: TMS assessment 24 hours after intervention.

5.1.4 Metrics

5.1.4.1 Robot-based metrics

Two different metrics quantified the performance of the user: SCORE and root mean squared error (RMSE). SCORE was calculated for each trial as the percentage of collected onscreen items, whereas RMSE was calculated by subtracting the performed trajectory from an ideal linear path between onscreen items. Note that it could be possible to collect all the onscreen items by performing a high error trajectory between them (see Figure 5.2 for an example).

SCORE and RMSE were calculated for two different sets of data:

a) evaluation post training repetitions, *i.e.*, the 10 last repetitions of each training day (see ROBOTIC TRAINING in Figure 5.1), in what we called POST-train values;

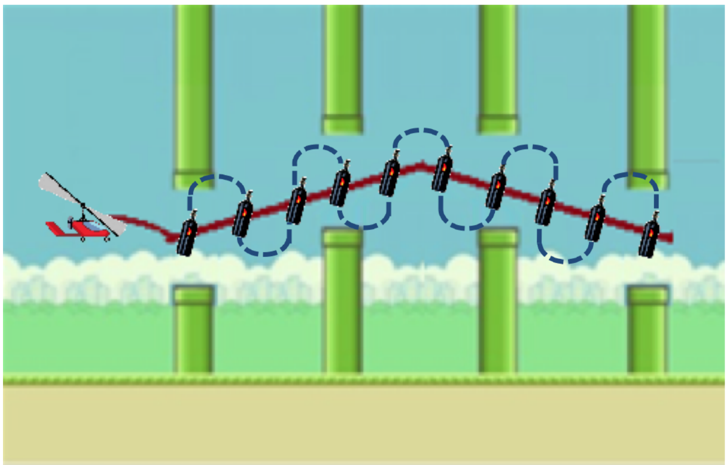


FIGURE 5.2: Trajectory example, with the best trajectory between items in continuous red line, and a high error trajectory between items (with 100 % SCORE as all the items are collected) in dotted blue line.

b) linear fit on the sequence of the 120 training repetitions (40 training repetitions per day, concatenated for the three days), and selected the values of the resulting linear fitting coinciding with the first (1) and last (120) repetitions, in what we called MOD (modulated) values: PRE-MOD and POST-MOD were the first and last values of the linear fit, respectively (See Figure 5.3).

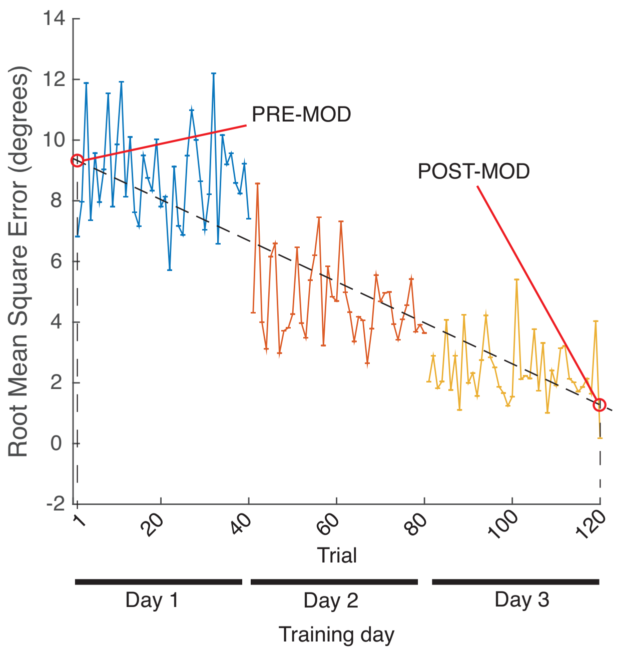


FIGURE 5.3: MOD metric calculation example, for RMSE.

5.1.4.2 Neurophysiological assessment

Corticospinal excitability was assessed by recording the MEPs elicited by a Magstim 200^2 TMS stimulator in single pulse modality in combination with a figure-of-eight double-coned coil. We followed the instructions by SENIAM [Hermens et al., 1999] to place the surface electromyography Ag/AgCl electrodes (22.225 x 34.925 mm, Vermed), recorded with a g.USBamp amplifier (g.tec), sampled at 24 kilohertz and high-pass filtered with a 20 Hz first order Butterworth filter.

In order to map the hot spot (place where tibialis anterior MEPs peak-to-peak amplitude is higher) on the scalp, several supra-threshold pulses were delivered nearby the vertex. The hot spot, inion and vertex were drawn with a permanent marker on a swimming cap, in order to ensure repeatability between sessions. After locating the hot spot, the resting motor threshold (RMT) defined as the stimulation intensity that elicits MEPs of approximate 50 μV peak-to-peak amplitude in five out of ten applied pulses [Temesi et al., 2014], was set for each participant. We recorded collaterally [Kamibayashi et al., 2009] tibialis anterior and soleus (SO) as well as rectus femoris (as a control muscle not involved in the robotic ankle task).

The assessment consisted on delivering 20 pulses to each of the volunteers at an intensity of 120 % of the RMT to elicit MEPs. The peak-to-peak amplitude of the MEPs was averaged. This assessment procedure was performed four times: 1) before the training of the first day (PRE); immediately after the training of the third day (last training, POST); 30 minutes after to evaluate plastic effects (POST30); and finally 24 hours after, in order to check lasting effects (POST24h). For a graphic schema of the study timeline, see Figure 5.1.

To check the suitability of the subjects for the TMS assessment procedure, it is important to pass a screening questionnaire. We elaborated an integrated screening form for the studies performed at our lab involving TMS and MEPs measurements, based on several previous questionnaires by other authors [Rotenberg et al., 2014, Keel et al., 2001, Rossi et al., 2011].

5.1.4.3 Satisfaction questionnaire

After the treatment, all the subjects overcame a Likert scale (1- Very unsatisfied; 2- Unsatisfied; 3- Not satisfied nor unsatisfied; 4- Satisfied; 5- Very satisfied) questionnaire for assessing the satisfaction level with the experimental procedure.

5.1.5 Data analysis

After examining with Shapiro-Wilk test, our data showed variables with normal distributions and variables violating the normality. Thus, for those without a normal distribution, we provide the results for non-parametric tests; and for those that present a normal distribution, we provide both parametric and non-parametric analyses.

First of all, we tested the correlation between SCORE and RMSE with a Spearman bivariate analysis (p value of 0.05), both for the evaluation metrics after each day training (POST-train), and for the PRE-MOD and POST-MOD along the 120 training modulated trials (40 per day); to check the relationship between metrics.

Our main hypothesis was tested using a Friedman test of differences among repeated measures along the study, finally evaluating the size effect with Average Spearman rho ($\overline{\rho_s}$). For the SCORE, we also performed a One-way repeated measures ANOVA, with Huynh-Feldt correction due to lack of sphericity (Mauchly's test), with partial squared omega (ω_p^2) for the size effect. This was done in order to evaluate the influence of the treatment on the performance in the task, and for this we tested the changes in SCORE and RMSE after the training (POST-train), and peak-to-peak MEPs amplitude.

Finally, to assess changes in the PRE-MOD vs. POST-MOD of the SCORE and RMSE on the modulated repetitions we used the Wilcoxon signed-rank test, evaluating the size effect by Cliff's δ test. We conducted also t-Student analyses, providing Cohen's d as the size effect.

5.2 Results

We found significant ($p < 0.05$) strong correlations ($\rho > 0.70$) in the evaluation ratings after each day training (POST-train), shown in table 5.1. See table 5.2 for the descriptive statistics.

TABLE 5.1: Spearman test for those correlations with a $\rho > 0.70$ and $p < 0.05$.

		RMSE	
		1st day	3rd day
SCORE	1st day	-0.89	
	3rd day	-0.76	-0.86

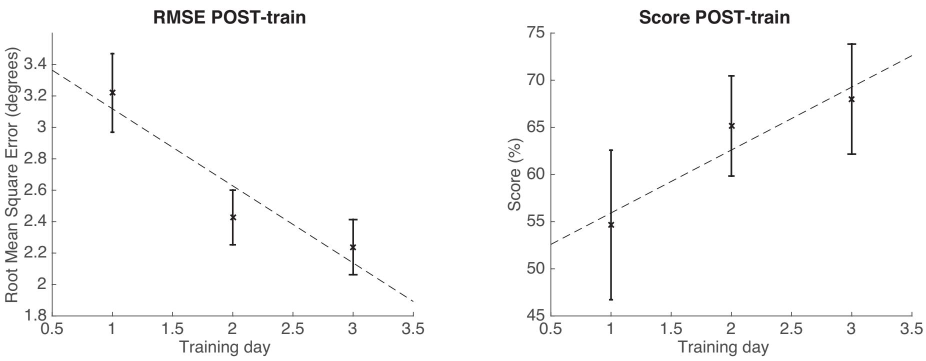
Friedman test rendered statistical changes ($\chi^2 = 9.39$; $p < 0.05$; $\overline{\rho_s} = 0.41$) for the SCORE; and also significant in the ANOVA ($F_{(1.18,10.60)} = 6.84$; $p < 0.05$; $\omega_p^2 = 0.35$). On the other hand, Friedman test results were not statistically significant for RMSE, see Figure 5.4.

In the case of TA MEPs peak-to-peak amplitude, Friedman test was statistically significant ($\chi^2 = 9.12$; $p < 0.05$; $\overline{\rho_s} = 0.22$); but not significant for both SO and RF, see Figure 5.5.

Table 5.2: Descriptive statistics for the variables analyzed for the group of healthy individuals.

		mean	median	standard deviation	min	max
RMSE POST-train	1st day	3.22	2.82	2.31	1.52	9.59
	2nd day	2.43	2.39	1.05	1.23	4.95
	3rd day	2.24	2.14	0.99	1.11	4.57
SCORE POST-train	1st day	54.65	54.25	19.53	15.50	84.50
	2nd day	65.15	62.25	9.92	55.00	82.50
	3rd day	68.00	64.75	11.97	54.00	87.00
RMSE modulated	PRE-MOD	4.02	3.65	1.77	1.62	6.86
	POST-MOD	1.99	1.79	0.95	0.98	4.05
SCORE modulated	PRE-MOD	43.54	40.15	18.34	24.07	80.11
	POST-MOD	67.84	66.77	9.77	54.92	85.05
TA MEPs	PRE	238.99	176.33	144.07	107.16	505.69
	POST	312.94	344.67	154.82	108.96	504.29
	POST30	281.59	296.33	111.02	107.32	411.23
	POST24h	403.56	385.64	222.82	114.94	807.08
SO MEPs	PRE	94.36	90.51	43.42	28.33	162.03
	POST	109.00	119.30	50.21	30.48	169.56
	POST30	99.35	100.20	44.19	29.41	176.05
	POST24h	107.46	115.84	50.21	31.87	198.76
RF MEPs	PRE	228.17	209.44	163.19	34.49	495.57
	POST	215.42	243.36	129.98	34.38	387.78
	POST30	190.06	146.14	171.15	22.50	555.03
	POST24h	236.82	210.45	164.92	31.45	487.19
Satisfaction		4.80	5.00	0.42	4.00	5.00

Wilcoxon Signed-Ranks test indicated that the median of the SCORE POST-MOD of the modulated training, median 66.77, was significantly higher than the SCORE PRE-MOD, median 40.15, ($Z = -2.60$; $p < 0.05$; Cliff's $\delta = -0.72$), and that the median of the RMSE POST-MOD of the modulated training, median 1.79, was significantly lower



(a) Mean and standard error of POST-train for RMSE per day.

(b) Mean and standard error of POST-train for SCORE per day.

Figure 5.4: Results for the RMSE and SCORE after each day training (POST-train) for the group of healthy individuals.

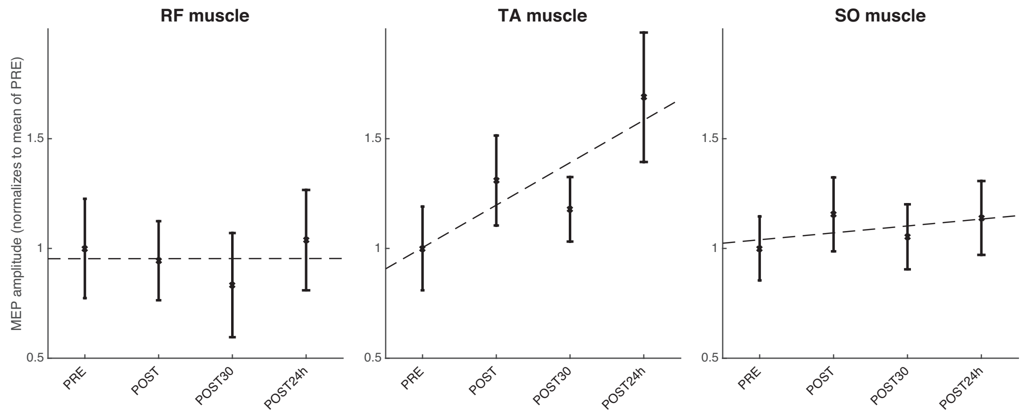


FIGURE 5.5: Results for the TMS assessment for the group of healthy individuals for the four evaluated moments, normalized to the mean of the evaluation before the intervention: before the full intervention (PRE), right after the full intervention (POST), 30 minutes after the POST (POST30), and 24 hours after the end of the full intervention (POST24h); for the muscles TA (tibialis anterior), RF (rectus femoris) and SO (soleus).

than the RMSE PRE-MOD, median 3.65, ($Z = -2.50$; $p < 0.05$; Cliff's $\delta = 0.76$). In addition, t-Student analysis rendered significant changes for both in RMSE ($t(9) = 3.05$; $p < 0.05$; Cohen's $d = 0.96$) and SCORE ($t(9) = -4.39$; $p < 0.05$; Cohen's $d = 1.39$).

The satisfaction questionnaire ranged 4.8 of 5 (being 5 Very satisfied), with a standard deviation of 0.42.

5.3 Usability case study with a stroke patient

We designed a usability case study to be tested with stroke patients. One stroke patient, age 37, participated in the case study. The patient suffered an haemorrhagic transformation of ischemic stroke, affecting the right middle cerebral artery, thus the most affected side is the left. The experiment with the patient was performed in the facilities, and under the supervision of the professionals, of *Centro de Referencia Estatal de Atención Al Daño Cerebral* (CEADAC). The patient signed the Informed Consent, acknowledging the risks and the inclusion criteria (he was previously examined by a physician, who validated the suitability for the training). These experimental procedures were approved by the local scientific committee in CEADAC.

We focused only on dorsiflexion torque patterns, because the patient was not able to avoid the full drop of the foot. Besides, the torque was modified (see Figure 5.6) to remove abrupt changes in the direction of the force exerted by the robot. We empirically set a maximum of 5 N·m.

The length of the protocol was modified to five days (replicating the protocol in [Asín-Prieto et al., 2018a]).

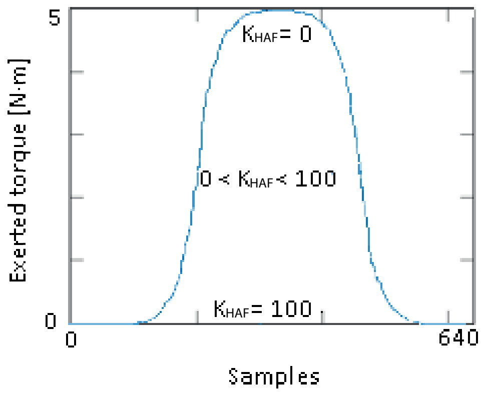


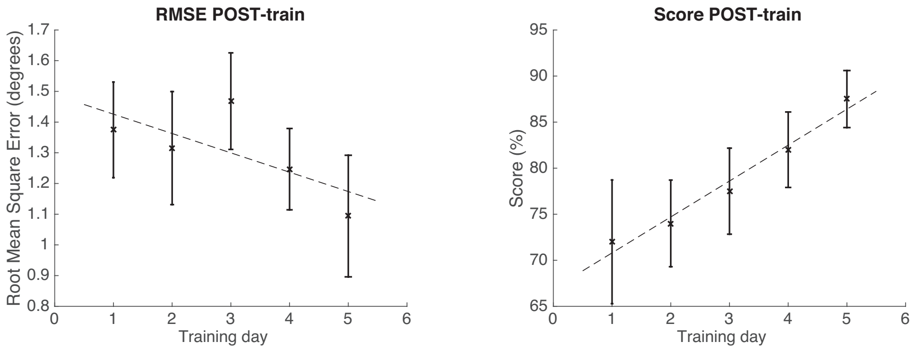
FIGURE 5.6: The figure shows the the torque to dorsiflexion (up) direction for the patient. The behaviour of the HAF module is depicted: 1) $K_{HAF} = 1$ prompts zero–torque control; 2) $K_{HAF} = 0$ normal torque control, so up to 15 N·m reference; and 3) K_{HAF} between 0 and 1, nearer to a zero–torque control the higher K_{HAF} is.

In addition to RMSE and SCORE after each day training (POST-train), we introduced two new metrics for the patient: ROM and velocity. Before and after the training for the second to the fifth day, the patient underwent a robotic evaluation of the possible ROM. This evaluation consisted on moving up and down a ball on the screen via dorsi-plantarflexion. The patient was asked to alternatively reach two horizontal lines (one up and one down), and the position of these lines was changed to the maximum reached in order to make the task more difficult. Although the separation between lines meant a wider ROM, the absolute position of them remained the same onscreen in order to be unnoticeable for the patient.

Additionally to these metrics, the clinicians at CEADAC performed a clinical evaluation at the beginning and the end of the week for the patient, before the first training session, and after the last one. In the rehabilitation process there are three main phases that need to be characterized: 1) initial assessment, to identify and measure the extend of the pathology; 2) planning, to assess the problem and establish the objectives; and 3) final assessment, after the treatment. In the functional assessment protocol developed in CEADAC, among the broad panoply of clinical functional scales that aim to provide an objective insight in the recovery process of patients, the clinicians focus on: Timed 10 meter walk, as a measure of gait speed; 6 Minute Walking Test -6MWT-, as a measure of resistance; Step Test, as a measure of dynamic balance; Timed Up and Go -TUG-test, that demands several potentially destabilizing maneuvers for the subject.

The same statistical analysis to that in the case of healthy volunteers was made in this case study for the SCORE and RMSE after each training session (POST-train).

The results for the case study rendered significant changes both in RMSE and SCORE POST-train (see Figure 5.7) with a Friedman test ($\chi^2 = 9.36$; p = 0.05; $\overline{\rho_s} = 0.14$) for the RMSE. The SCORE presents normality, so we performed a Friedman test ($\chi^2 = 12.07$;



(a) Mean and standard error of post RMSE per day.

(b) Mean and standard error of POST-train SCORE per day.

FIGURE 5.7: Results for the RMSE and SCORE POST-train, after each day training for the patient.

$p < 0.05$; $\overline{\rho_s} = 0.22$), and an ANOVA (corrected with Huynh-Feldt, non significant, $p = 0.09$). See table 5.3 for the descriptive statistics.

TABLE 5.3: Descriptive statistics for the RMSE (degrees) and SCORE (%) POST-train for the patient.

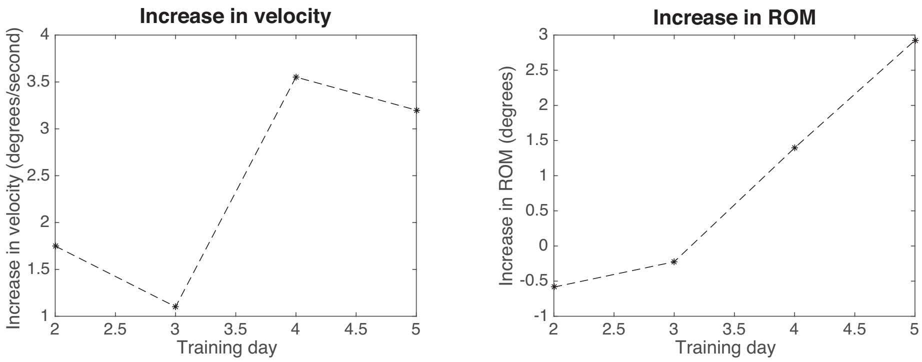
		mean	median	standard deviation	min	max
RMSE POST-train	1st day	1.37	1.21	0.49	0.65	2.45
	2nd day	1.32	1.29	0.58	0.12	2.36
	3rd day	1.47	1.19	0.50	1.05	2.43
	4th day	1.25	1.06	0.42	0.97	2.31
	5th day	1.09	1.00	0.63	0.31	2.22
SCORE POST-train	1st day	72.00	72.50	21.24	35.00	100.00
	2nd day	74.00	75.00	14.87	50.00	100.00
	3rd day	77.50	77.50	14.77	55.00	100.00
	4th day	82.00	85.00	12.95	55.00	100.00
	5th day	87.50	90.00	9.79	75.00	100.00

We provide in Figure 5.8 the results for the evaluation of the ROM and velocity before and after each training session (from the second to the fifth day). There is an increase in all the days in ROM, but not in velocity (there is a decrease between the third and the second day, and between the fifth and the forth, although there is a net increase).

Table 5.4 presents the improvements on the clinical scales, before and after the full treatment.

TABLE 5.4: Clinical scales before the beginning and after the end of the full five day treatment.

	Before	After
Timed 10 metre walk (metres/second)	1.6	1.7
6MWT (metres)	455	465
Step test (repetitions)	7	11
TUG (seconds)	9.50	8.52



(a) Velocity increase per day, values: 2nd day - 1.75; 3rd day - 1.10; 4th day - 3.55; 5th - 3.20.

(b) ROM increase per day, values: 2nd day - -0.59; 3rd day - -0.23; 4th day - 1.40; 5th - 2.93.

FIGURE 5.8: Results for the RMSE and SCORE POST-train, after each day training for the patient.

The satisfaction questionnaire for the patient ranged 5 of 5 (being 5 Very satisfied).

5.4 Discussion

We aimed to explore the validity of the combination of the robotic tool and video game we designed for promoting motor learning in a therapy protocol involving autonomously customized control. We have developed this video game for enhancing adherence and engagement, by providing the control of the robot with the performance to modulate the task difficulty. We approached this objective by providing perturbations to the user's ankle while asked to follow a trajectory depicted as a sequence of collectible onscreen items. The magnitude of the perturbations was modulated in function of the performance, *i.e.*, the number of collected items, making the task more difficult if the performance increased, and vice versa.

This reward system based on providing autonomously customized hardness on the task to the user potentially promotes learning. We also computed the error understood as the difference between the most efficient trajectory between onscreen items and the actual performed trajectory, and moreover, we evaluated other markers (TMS for the corticospinal excitability on healthy individuals; clinical scales, range of motion, and velocity on the patient; and satisfaction with the process of intervention) to support our findings.

In brief, in this longitudinal study we have integrated, among other assessment tools, the use of TMS for the assessment of activity-dependent motor learning, after undergoing a training with a robotic tool and a video game. Regarding this technique, although there are limitations and results are not consistent when extrapolating corticospinal excitability improvement to learning processes in rehabilitation [Carson et al., 2016], several recent studies point that an increase in corticospinal excitability may be related to an improvement in motor learning [Naros et al., 2016, Kida et al., 2016, Mrachacz-Kersting et al., 2019, Christiansen et al., 2018, Mawase et al., 2017, Raffin and Siebner, 2018], and moreover, there is a relationship between the improvement in the metrics in the robotic therapy, motor learning, and corticospinal excitability enhancement in healthy subjects [Perez et al., 2004]. For this reason, we can conclude that TMS is a reliable and valid technique to assess the corticospinal excitability in our study.

Regarding the validation study in healthy volunteers, for the POST-train metrics, *i.e.* after each day of training, we found significant improvement in the SCORE (medium effect size -according to Koltrlik and Williams [Kotrlik and Williams, 2003]- for the Friedman test, but large for the ANOVA -according to Field [Field, 2018]-), but not in the RMSE. However we found a strong inverse correlation between SCORE and RMSE (Spearman's $\rho > 0.70$), which would imply that similar results to those already found in [Asín-Prieto et al., 2018a] are expected, where a duration of five days for the treatment lead to significant changes in both metrics.

In contrast to the POST-train metrics, we found significant improvements along the training, *i.e.* the MOD variable, for both the SCORE and RMSE (large size effect for Wilcoxon –according to Romano et al. [Romano et al., 2006]– and t tests [Kotrlik and Williams, 2003], for both metrics). This fact may imply also that this metric is more accurate to assess the changes in volunteers for SCORE and RMSE, as the controller (and thus the torque applied to the ankle) is autonomously modulated via HAF algorithm, rather than being the maximum applicable torque (15 N·m), as it is for the POST–train metric.

We also found a significant increase in TA MEPs peak-to-peak amplitude (small effect size [Kotrlik and Williams, 2003]), supporting that an increase in performance has a relationship with corticospinal excitability. These corticospinal changes do not show muscle specificity depending on the task, as our training involves only the ankle and we have not found statistical changes in RF (control muscle) but neither in SO. Consequently, we only can conclude that our training has increased TA excitability, but we cannot explain the reasons why the control muscle and SO have not increased. On the other hand, SO has not significantly increased probably due to the fact that the robot controller is in favour of gravity, and thus the force to move the robot downwards requires less muscle activation than that for TA. Another possible explanation could be that TA, according to Brouwer and Ashby's findings [Brouwer and Ashby, 1992], presents a higher corticospinal projections density than the rest of the lower-limb muscles, and thus it may render easier to assess its excitability. In this sense, corticospinal projections to TA in comparison to the rest of lower-limb distal muscles, are comparable to those at upper-limb level [Brouwer and Ashby, 1990], and thus we could say that our results are consistent to those in the literature for upper-limb robotic approaches [Ramos-Murguialday et al., 2014, Kraus et al., 2016].

In the case study (with the stroke patient) results, we found significant improvements in the performance (both in the SCORE and the RMSE) after each day training with the Friedman test (medium effect size [Kotrlik and Williams, 2003]) but non significant with the ANOVA ($p = 0.09$). The significant results of the Friedman test are consistent not only with the results of our healthy sample, but also with already presented literature [Goodman et al., 2014, Reinkensmeyer and Patton, 2009, Krakauer, 2006, Patton et al., 2001], thus confirming our hypothesis of usability in the case study. Although we have provided some data on the performance for this patient, our main result here is to validate the usability with a patient.

When we compared the ROM and velocity before and after each day training, we found that there is a net increase both in velocity and range of motion along the days, although in the velocity there is a sawtooth shape profile (third and fifth day presented a lower increase than second and fourth respectively). Nonetheless, as higher ROMs would inevitably render lower velocities, the sawtooth-shaped behaviour of the velocity could be explained by this phenomenon. If these data imply a behavioral improvement in the control of the ankle, the variation occurs together with that of the clinical scales used to assess the improvement after the treatment. Consequently, we can consider that these changes in ROM and velocity tend to improve like the clinical scales.

As reported by the Likert satisfaction scale, both studies lead to full satisfaction of the participants. We found the viability of using this treatment in patients, as the patient ranged the intervention similarly to the range given by the healthy group.

Our objective was to validate our proposed therapy as a potential tool for increasing motor learning on healthy individuals.Thus, taking into consideration all these results, our hypothesis has been confirmed in the POST-train metric for the SCORE and for the TA excitability; and for the MOD variables. Regarding RMSE, our hypothesis has not been confirmed, probably due to the short duration of the treatment. On the other hand, for the case study with the stroke patient, both SCORE and RMSE have changed as hypothesized in the design of the study.

Finally, we conclude that providing combined visual and haptic adaptive feedbacks via our proposed integrated tool, comprising a grounded ankle exoskeleton and a video game with autonomously controlled difficulty, elicits improvements in the performance, and also positive changes in the excitability of the target muscle. This conclusion renders our proposal as a potential rehabilitation tool. Furthermore, we have demonstrated the viability of applying this treatment approach in a usability case study with a stroke patient, and propose, as a future work, performing a study with a wider number of patients, and thus checking if our results for healthy individuals could be translated into a more representative sample of stroke subjects.

This novel ankle training may improve the stroke rehabilitation, it also could help other pathologies like spinal-cord injury [Asín-Prieto et al., 2016b], cerebral palsy [Lambrecht et al., 2014, Lefmann et al., 2017], or other lower limb movement disorders [Reinkensmeyer et al., 2004, Calabro et al., 2016].

5.4.1 Limitations

The main limitation that affects our usability case study is that we only enrolled one stroke subject. Although there is an increase in the performance on the task in all the presented metrics, we cannot assume that these improvements are only due to our treatment, as the patient overcame his daily therapy with physio- and occupational therapists. Nonetheless, the clinical scales rendered a good prospective of the integrated therapy including both the regular therapy delivered at the clinic and our proposed treatment.

To avoid too long daily experimental sessions, we discarded the option of assessing the corticospinal excitability before and after each day training in our healthy sample. Thus, we cannot isolate the daily effects of the robotic tool training. Regarding the neurophysiological changes, in order to improve the assessment setup it could have been possible to apply other techniques in order to test where the excitability changes were located in the nervous system. For example, we could have checked spinal reflexes or paired-pulses TMS protocols, *i.e.* check if the changes are spinal, cortical, or likely at both levels. Another future perspective for this study is to apply complement neurophysiological assessments to check the location of the neuroplastic changes.

In this vain, the lack of changes observed in the corticospinal excitability in SO nor in RF, renders us unable to conclude that the robot training is the responsible for changes in distal but not proximal muscles. To overcome this issue, we would need a more specific control experiment, *e.g.* with the comparison of the changes in these three muscles with a protocol focused on proximal muscles vs. another for distal ones (the work presented in this chapter). Furthermore, the lack of significant changes in our results, may imply that the fact that SO presents less density of corticospinal projections than TA [Brouwer and Ashby, 1990, Brouwer and Ashby, 1992], and thus, SO might be a better muscle for the hot spot. As SO would require more stimulation intensity, TA would consequently be recruited as well, potentially providing a more adequate approach for the simultaneous assessment of both distal muscles.

Chapter 6

Conclusions and future work

In **chapter 1**, I explained how the gait is originated, the different mechanisms involved in the process, and the main alterations that a person may suffer such as paresis, muscle weakness and lower limb paresis, as a consequence, among others, of stroke or spinal cord injuries. Multiple pathologies, with high prevalence in today's society, have been described that limit motor capacity. I also described the different devices in the literature, with their features and lacks, that motivate the work that I have exposed in the following chapters

Furthermore, this chapter evidenced that human gait is much more than only the function that allows ambulation. It is a fundamental function for the integral development of humans from the very first years of life, since it influences all daily living activities, in the personal, work and familiar aspects. It allows interaction with the environment, but also constitutes a non-verbal communication mode, through which ideas or mood can be transmitted. Hence, the total or partial loss of mobility conditions the human not only in a physical dimension, but also at psychological and cognitive levels, in addition to the economic implications that this implies in the high health costs that it entails.

In **chapter 2**, I covered the explorative journey followed prior to developing the proposed rehabilitation robotic tool. First, I cursorily presented the robotic tool used for the development: MACCEPA actuators.

Then I presented the study we published with the H2 robotic exoskeleton and the first successful implementation of the tacit learning algorithm for wearable robots: tacit adaptability. I provided evidence on how this algorithm was able to adapt a rigid position controller with rigid actuators to user intentions, thus providing joint stiffness tuning. Furthermore, I also provided the results on speed tuning with this approach.

I then presented two studies with this approach on a position controller on MACCEPA, based on the translation of tacit adaptability algorithm to be used with compliant actuators: 1) on the testbench mimicking static and dynamic conditions, modulating a fixed trajectory to users' intentions; and 2) with healthy users walking on the treadmill, showing the modulation of the stiffness of the actuator, without the use of torque sensors or complex models. Furthermore, the device felt confortable to walk and interact with for all the volunteers.

In **chapter 3**, I explored torque production with the rehabilitation robotic tool, and developed the basic framework, on which I based the development of the final control and visual paradigm strategies. I provided evidence that the proposed therapies standing and wearing the robot did not negatively influence the normal muscular activation seen in overground walking. I showed that we were able to enhance tibialis anterior activation and promote an after effect adaptation, that vanishes in time when the effect is removed. Although we were unable to promote the effect we wanted on gastrocnemius medialis in stance, I have provided reasoned explanations of what could be the cause, resembling a body weight supported exoskeleton.

In **chapter 4**, I have exposed the actual development of the final tool, with tacit adaptability applied to a torque-controlled MACCEPA ankle actuator, modulating tacit adaptability value with a therapy-intrinsic metric: the performance on the video game, and coining the term Haptic Adaptive Feedback (HAF) to name this new feedback paradigm. I showed that this paradigm led to an improvement in the performance for all the volunteers, and concluded that modulation techniques led to improved performance. The implementation of tacit adaptability on the video game feedback approach led to an improvement of the performance on a healthy individual.

In **chapter 5**, the proposed protocol involved the presented and preliminarily demonstrated autonomously customized control. We developed the video game for enhancing adherence and engagement, by providing perturbations to the user's ankle while asked to follow the trajectory. We provided evidence of motor learning in healthy individuals with increased performance in the video game, results endorsed by increased corticospinal excitability. In the case study with one stroke patient, we found the tool was potentially usable in the clinical scenario. All volunteers (healthy and patient) reported high levels of satisfaction with the protocol.

To sum up, in this dissertation I have thoroughly described the development of the robotic tool, and provided evidence of the usability, usefulness, and success of the proposed training protocols.

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