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Table of Contents

Brain activity dependent neuroprosthetic for cycling task in stroke patients: Feasibility study.

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***Abstract*—Research on lower limb motor rehabilitation is generally split into two types of interventions. One is through neuroprosthetics and others through neurorobotics. These interventions can benefit from the nervous activity dependent plasticity. Several studies have been done related with this issue and they have contributed to knowledge about how to help patients with stroke. In the present work, we show preliminary data of a pilot study in two patients with stroke who underwent a treatment with neuroprosthetics and cycling. The same treatment was applied with a stimulation timing dependent on the brain activity (experiment 1), and without this temporal association (experiment 2). The results show a greater increase of excitability in the cortico-spinal pathway of the patient who underwent the brain activity-dependent cycling treatment. In addition, we discuss some changes made in the intervention after testing in patients as an improvement on it.**

I. Introduction

STROKE patients [1], as a consequence of their brain injury, if they survive the insult, may have affected the cognitive system, as well as the activities of daily life among others. One of the affectations that most limit and affect patients is the loss of mobility of their limbs, since it makes them lose independence and the ability to walk if it affects the brain areas related with the lower limb.

One of the strategies in neurorehabilitation applied to the injuries affecting the sensory-motor system is neuroprosthetics. These techniques generally use electrical current to restore function of the nervous system [2]. One of the techniques used in this sense to assist or rehabilitate limbs with a lack of mobility is functional electrical stimulation (FES) [3]. The technique consists of placing surface electrodes on the skin. Anode and cathode are placed over the target muscle to locate the stimulation on it. In this way, it is possible to recruit the nerve fibers that innervate it, achieving both its contraction and the generation of somatosensory afferences.

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One of the muscles of interest for both walking and cycling is the Rectus femoris. The authors of the mentioned publication [4] used it to assist the cycling, stimulating quadriceps, hamstrings, gluteus maximum, and tibialis anterior of both legs with FES. In this sense, they achieved improvements in the lower limb movement clinical scales after the treatment.

On the other hand, the authors of the following study [5] use the potentials recorded with electroencephalography (EEG) called movement related cortical potentials (MRCPs) to associate them with electrical stimulation in the common peroneal nerve of the paretic leg of stroke patients. In this way, they achieve improvements by associating brain activity with afferent stimulation of the lower limb. Following this line, the authors showed the changes in the excitability of the cortico-spinal pathway as a marker of plastic changes that support the clinical improvements tested in these patients. The way to assess the changes in the cortico-spinal pathway of these patients is via the use of transcranial magnetic stimulation (TMS) [6]. The modality of single pulse helps us to check the state of excitability of this pathway, and if there have been changes related to a given experimental intervention.

The present study shows the results of a pilot trial in two stroke patients. An intervention with brain activity-dependent stimulation with FES while cycling was applied, and we show the changes in cortico-spinal excitability, as well as the feasibility of using this intervention in these patients.

II. Methods

A. Patients

Two stroke patients from the hospital La Fe (Valencia), and previously having approved the hospital ethics committee, were selected as they fulfilled the requirements to do the experimental intervention that will be explained below.

B. TMS Assessment

The sEMG electrodes were placed to record the motor evoked potentials (MEPs) of both rectus femoris. Once the place of stimulation was located on the scalp (hotspot), the resting motor threshold (RMT) was recorded and twenty pulses were applied at 120% of that RMT in each of the assessments. For this evaluation, an eight-shaped (conical)

coil and a single pulse stimulator were used.

C. Setup

The muscles recorded and stimulated in the study are both rectus femoris, since they are very relevant to the task. Moreover, we intended to know if reducing the number of muscles stimulated during cycling would produce potentially beneficial changes. For this reason, surface electromyography (sEMG) electrodes were placed over these muscles in both legs.

Once cortico-spinal excitability was assessed as explained in point B, we proceeded to apply the experimental treatment consisting of 40 calibration trials to know the precise time in which the patient will be stimulated with the FES. The MRCPs were recorded with EEG, and filtered with a Butterworth 1st order high-pass filter (0.05 Hz). We focused our analysis on the channels around Cz.

One patient undergone the experimental treatment based on brain-state dependent stimulation, as explained in the previous paragraph (experiment 1). For the other patient we applied FES on rectus femoris directly after a visual countdown that indicated the moment to start cycling (experiment 2). Summing up, depending on the applied protocol, the FES stimulation was always applied at different time of cycling (on experiment 1 depending on EEG, and on experiment 2 just after the visual countdown end). On the experiment 1, FES was applied in the time when the offline averaged negative peak of the MRCPs was calculated (in relation to the visual countdown). In the experiment 2, FES was immediately applied after the end of the countdown. As previously said, this countdown indicates each patient to be ready for cycling.

Once the cycling task with the stimulation was completed, the cortico-spinal way was again assessed with TMS, and after 30 minutes to check the long-term effects. In such a way, we recorded the cortico-spinal excitability PRE-, POST-, and POST 30 'after treatment. Fig. 1 summarizes the general procedure of the experimental session.

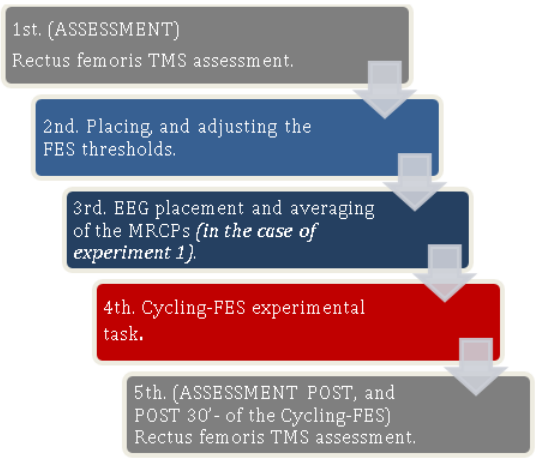

Fig. 1. Flowchart of the experimental intervention process.

III. Results

Fig. 2 shows how the peak-to-peak amplitude of the MEPs in the experiment 1 patient increases after the experimental treatment. Regarding the experiment 2 patient, no changes were observed.

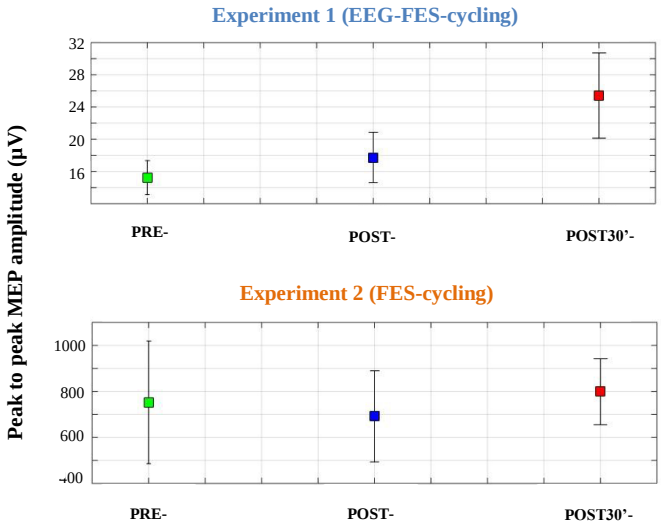

Fig. 2. MEPs amplitude (mean +/- SD) of the affected Rectus femoris

IV. Conclusions

The setup has been proven applicable in stroke patients with the characteristics that have been exposed. Since it allows patients to perform the task of cycling without added difficulties. On the other hand, experiment 1 in which FES is applied in the task of cycling depending on brain activity, has shown increases in cortico-spinal excitability that suggest that it could improve the intervention with only FES and cycling.

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Analysis of video-oculographic registers for the discrimination of Parkinson's disease

J-A. Gómez García, L. Moro-Velázquez, J-I. Godino-Llorente

***Abstract*— This paper explores the usefulness of features extracted from video-oculographic recordings for the discrimination of Parkinson's disease. Experiments are performed on a dataset containing eye tracking registers of age-paired parkinsonian and control subjects during a visual exploration task. The total saccadic excursion -measuring the extent of the exploration area- and the number of saccades are employed to differentiate between populations. In particular, the total saccadic excursion achieved an area under the ROC curve of 0.98, indicating that parkinsonian and control subjects differ in terms of the extension of exploration during the proposed visualization task. These preliminary results suggest the appropriateness of using video-oculography to analyze Parkinson's disease, and the potentiality of signal processing techniques for automatic detection labors.**

I. INTRODUCTION

Parkinson's Disease (PD) is a chronic degenerative disorder that affects 1% of the population over 60 years. However, to date, there are not early and non-invasive markers of the disease, still being autopsy the gold standard for the actual confirmation of the impairment. It has been stated that the study of eye movements provides one of the most important windows to understand function and dysfunction of human brain [4], as erratic eye movement can be useful indicators of the presence of certain neuronal disorders. Indeed, literature reveals that ocular movements in PD subjects are affected even in pre-symptomatic stages of the disorder. For instance, several studies acknowledge dysfunctions in the production of fixational and saccadic movements [1][4] [8] [6]. Similarly, it has been found that during visual exploration of simple images, PD patients reduces the number and amplitude of saccades while increasing the duration of fixations. On more complex images, there exist a certain compensation. Notwithstanding, it is stated that in general terms the exploration areas are smaller in PD patients than in control populations [5].

With these antecedents in mind, the aim of this paper is to employ *Video-oculographic* (VOG) recordings and signal processing techniques to differentiate between control and PD populations using data recorded during a visual exploration task.

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II. SETUP

A. Corpus

A subset of a corpus recorded at *universidad politécnica de Madrid* is employed in this paper. The dataset has been recorded in collaboration with the otorhinoaringology and neurology services of the *Gregorio Marañón hospital* in Madrid, Spain. The corpus contains binocular eye tracking recordings of subjects during several experimental paradigms elliciting saccades, fixations, smooth pursuits, etc. However, only one paradigm involving the visual exploration of an image is considered in this paper. Registers have been acquired binocularly using the Eyelink 1000 Plus system with a sampling rate of 1000 Hz, and employing a chin rest to stabilize the head during the recording process. For this paper purposes, registers of 9 subjects with idiopathic PD (3 women and 6 men) whose average age is 68 years and in stages II and III according to the Hoehn & Yahr scale are employed for experimentation, next to registers of 10 control subjects (5 women and 5 men) whose average age is 69. All of the patients were under pharmacological treatment and ingested their medication 2 to 5 hours before the data acquisition procedure.

B. Methods

Registers have been processed using Matlab and the edfimport tools [7]. The events provided by the eye tracker (saccades, fixations, ...) are used for the calculation of the *total number of saccades* and the *total saccadic excursion*. The latter is computed as the summation of all the individual saccadic amplitudes, being defined as follows:

$$d_i = ||(x_i^0, y_i^0), (x_i^1, y_i^1)||$$

$$\text{total saccadic excursion} = \sum_i d_i$$

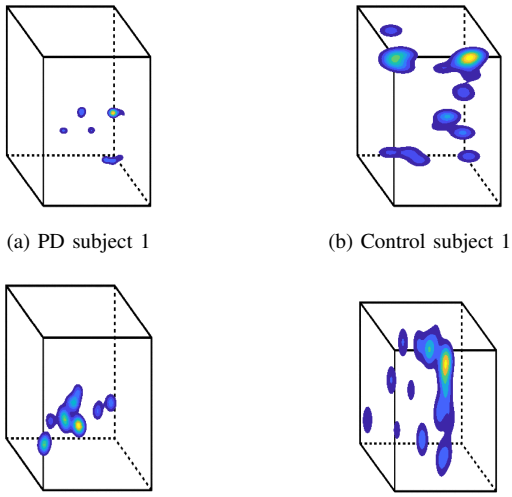
where (x_i^0, y_i^0) is the coordinate where a saccadic event i starts, and (x_i^1, y_i^1) where it ends (it becomes a fixation).

Boxplots and the *Receiver-Operating Curve* (ROC) are employed to visually assess the discriminatory capability of these two features. Similarly, the *Area Under the ROC curve* (AUC) is utilized to quantify the potential to differentiate between populations.

III. RESULTS

Firstly, heatmaps of PD and control subjects are presented in Fig. 1. As observed, the exploration areas of the PD subjects are smaller that those of the controls, being mostly composed by fixations. By contrast, the control subjects

present a larger number of saccadic events, and the exploration of a larger extension of the image.



(a) PD subject 1 (b) Control subject 1

(c) PD subject 2 (d) Control subject 2

Fig. 1: Heatmap of the exploration areas of by PD (left) and control (right) subjects during the visualization task.

Next, a boxplot illustrating the distribution of the two proposed features is presented in Fig. 2. As observed, control subjects exhibit a larger number of saccades and a larger total saccadic excursion compared to the PD population. This provides numeric evidence of the observations previously made on the heatmaps. The boxplot also serves to illustrate the potential capabilities of these two features to disregard between both groups, as shown by the two differentiated -and almost non-overlapping- boxes of the two classes.

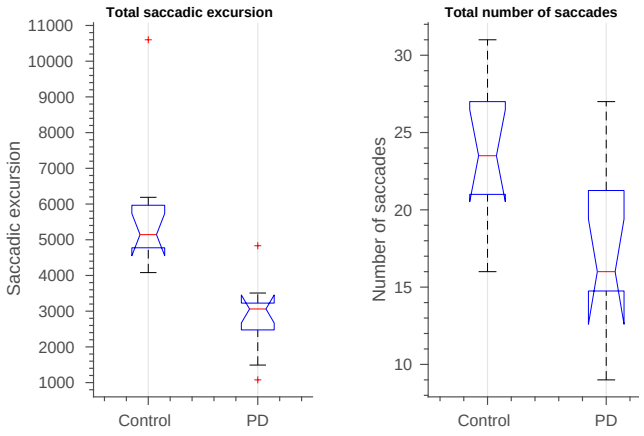


Fig. 2: Boxplot showing the distribution of the total saccadic excursion (left) and the total number of saccades (right).

Finally, Fig. 3 presents the ROC curve of the two proposed features. The corresponding AUC for the total saccadic excursion is of 0.98, whereas for the total number of saccades is of 0.86. The curve as the aforementioned values confirm the discriminatory capabilities of these two features, but most specially of the total saccadic excursion.

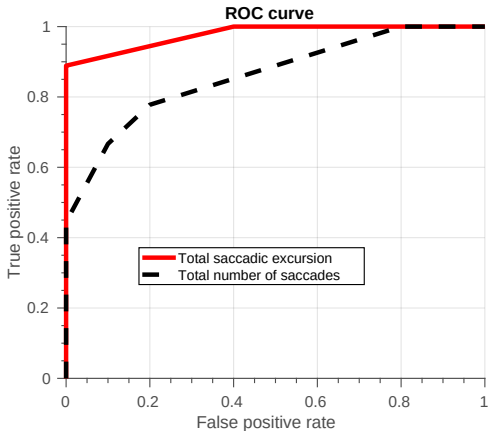


Fig. 3: ROC curve illustrating the discriminatory capability of the proposed features.

IV. Conclusions

This paper has presented preliminary results of two features with potential to be used in labours of automatic detection of PD using VOG recordings. It has been found that in general terms the excursion of PD patients is smaller that those of control subjects, having as well a decreased number of saccadic events. This is in line with the observations previously made in other works in the literature [8]. These simple features have served to illustrate the potential of using VOG for the analysis of PD. It also constitutes a first step towards the analysis using more robust signal processing techniques for the automatic detection of PD.

In the future we will explore the usefulness of other types of ocular movements such as smooth pursuit or optokinetic reflexes for the automatic detection of PD, as well as its combination to other types of biosignals.

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Review of the rationale behind mechanical tests for active implantable medical devices towards the mechanical testing of eAXON microstimulators

Aracelys García-Moreno and Antoni Ivorra

***Abstract*—The eAXON microstimulators, as any active implantable medical device (AIMDs), experience repeated mechanical stresses in the corrosive body environment that can affect the devices' mechanical properties and lead to failure. Mechanical tests represent an ethical method to reduce animal tests and reveal mechanical failures of AIMDs in a short-term. In this review, diverse publications were explored, focusing on those describing mechanical tests performed in AIMDs containing leads. The purpose was to try to find the rationale behind the tests and validate the approaches followed to design mechanical testbeds and protocols. Publications concur that tensile, fatigue and fracture tests are fundamental, and these tests must replicate *in vivo* conditions and mimic real-life scenarios. However, many publications lack the details of the rationale for the design of the mechanical tests.**

I. Introduction

IMPLANTABLE electrical stimulation systems based on wireless stimulators represent a minimally invasive alternative to currently available centralized systems for neuroprosthetics and for neuromodulation therapies.

The eAXON project (Fig. 1) envisions a dense network of addressable single-channel wireless microstimulators that we refer to as eAXONs (short for "electronic axons"). These devices will be injectable and will consist mostly of flexible materials. Their operation is based on electronic rectification of inert high frequency currents applied through epidermal electrodes. This innovative stimulation method allows miniaturization to submillimeter dimensions, which has been restricted in current technologies by the use of batteries and inductive coupling for power supply [1][2].

Between the components of an AIMD system (Fig. 2), the leads, which electrically connect the electrodes to the central units, are the most likely to fail due to the mechanical stresses and the extreme physiological conditions [3]. eAXONs are like small leads and will experience repeated mechanical stresses in the corrosive body environment that can affect their mechanical properties and lead to failure.

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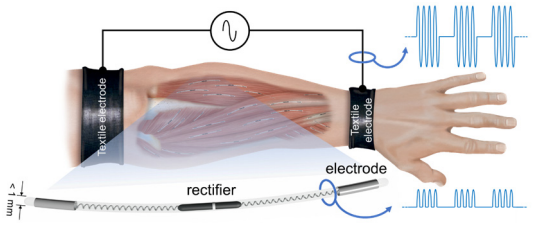

Fig. 1. The eAXON technology consists of a dense network of addressable single-channel wireless flexible injectable microstimulators. Externally applied inert HF currents are rectified by the eAXON microstimulators to generate LF stimulation currents.

In vivo tests are mandatory to identify potential mechanical problems and validate the robustness of AIMDs. However, these trials require long-term complex designs for statistically relevant results. Mechanical test benches and accelerated protocols represent an ethical method to reduce animal tests. These tests may reveal failures that simulations do not show and provide short-term affordable results [4].

As a first approach to the design of mechanical tests for the eAXONs, in this work we have reviewed and analyzed standards established by regulatory agencies and organizations and tests proposed by independent groups for testing the mechanical robustness of AIMDs trying to find the rationale behind them and validate the approaches followed to design mechanical testbeds and protocols.

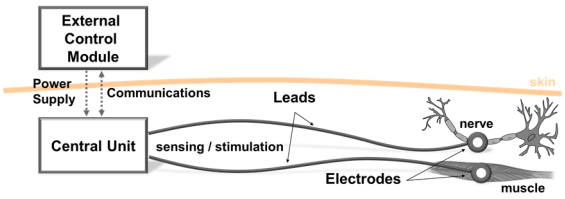

Fig. 2. Components of an AIMD system. Active implantable medical devices (AIMDs) are partially or totally introduced into the body by clinical intervention. Their functioning requires a source of electrical energy or power that is not generated by the body or by gravity [5].

II. Methods

Standards and guidance documents established by regulatory agencies and organizations, journal and patent databases, and technical books and websites were explored. Search terms included leads, coils, intramuscular, electrical stimulation, electronic implants, active implantable medical devices, mechanical tests and properties, fatigue and fracture, stress and strain. Documents describing mechanical tests performed in AIMDs were selected, including those

TABLE I
STANDARD TEST METHODS

Test	Standard	Application
Conditioning and test baths	[6]	Cardiac pacemakers Cochlear implant
Sterilization	[7]-[10]	Cardiac pacemakers Cochlear implant
Uniaxial tensile	[6][11]	Cardiac pacemakers Cochlear implant
Flex fatigue (fatigue and fracture)	[12] [13] [14]	Cardiac pacemakers Implantable defibrillators Cochlear implant

proposed by independent groups, and the analysis was focused on those containing leads.

III. RESULTS

Environmental and mechanical tests should reproduce real-life failure modes at accelerated conditions to obtain reliability results in a reasonable period. However, the correlation between approximate number of cycles along years of service and cycles in a testing period might require more than a simple mathematical translation [4]. Tables I and II show the most relevant tests performed in AIMDs.

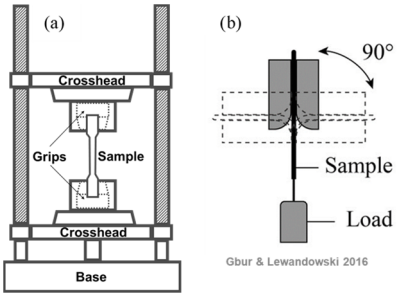

Fig. 3. Standard test methods. (a) Uniaxial tensile test of strength based on Hooke's law. (b) Flex fatigue test (tension and compression) based on Weibull analysis of MP35N® reference test coils.

IV. DISCUSSION

We were surprised to find out that in many publications the rationale for the design of the tests is very poorly detailed. Publications concur that tensile, fatigue and fracture tests are fundamental for the mechanical validation of AIMDs (Fig. 3), and that these tests must replicate *in vivo* conditions and mimic real-life scenarios, considering that, in the corrosive body environment, stress can induce chemical changes and lower the strength of the materials.

In accelerated tests, bending radius, angles, loads and/or cycling frequencies are increased to cause higher stresses and failure in a shorter time. Although this can affect fatigue limits in the same materials and devices for similar stress and strain, *in vivo* failure modes and fracture morphologies should be reproduced at accelerated conditions.

Some publications indicate the use of modelling and simulations to establish stresses and strains. Furthermore, test benches should reproduce identified AIMDs' failure modes depending on body location, materials and interfaces. We believe this is a valid approach for the preliminary design of the tests. However, we also believe that the analysis of failures in *in vivo* tested AIMDs must lead to the design of testbeds that emulate their causes, particularly in cases in which failure modes were not anticipated.

TABLE II
AD HOC TEST METHODS

Test	Source	Application
Three-point bending	[15]	BION microstimulators
Repetitive bending & loading	[15]	BION microstimulators
Bending	[16]	Implantable leads
Unidirectional bend fatigue	[17]	Cardiac leads
Rotating-bending fatigue	[18]	Intramuscular electrodes

V. CONCLUSION

This review and analysis of the rationale behind mechanical tests for AIMDs establishes the basis for the development of mechanical test benches specifically designed for the validation of eAXON microstimulators.

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A Feedback System to Characterize and Target Altered Motor Control in Cerebral Palsy

Alyssa M. Spomer, Nick A. Baicoianu, and Katherine M. Steele

Abstract— **Biofeedback has become increasingly popular in the field of rehabilitation for neuromuscular disorders, as it provides real-time, subject-specific measures and facilitates targeted practice for populations that are inherently heterogeneous. However, despite myriad successful implementations, real-time biofeedback has not been investigated as a method for quantifying neuromuscular control complexity, an application which may aid clinicians in developing successful intervention plans for improved patient mobility. Here, we describe the development of a near real-time system which quantifies subject-specific motor control complexity using streamed electromyography data and presents feedback to the user. The developed system is currently in use to better understand the plasticity of motor control patterns and the impact that real-time feedback can have on selective motor control modulation. The results of future analysis will guide investigation into the efficacy of incorporating real-time motor control feedback into rehabilitation to aid intervention planning and improve mobility outcomes for individuals with neuromuscular disorders.**

I. INTRODUCTION

Cerebral palsy (CP) is a non-progressive neuromuscular disorder caused by a traumatic brain injury occurring at or near the time of birth which typically affects an individuals motor control. Given the inherent uniqueness of brain injury, intervention planning and rehabilitation aimed at improving mobility in CP has been traditionally challenging. Without tools to quantify neurological variability, clinicians commonly rely on subjective metrics which often results in interventions that prove inconsistent or unsuccessful at restoring function [1][2]. Real-time biofeedback has become increasingly popular in the field of neuromuscular rehabilitation as a means of individualizing treatment planning and facilitating targeted practice to promote neural plasticity [3]. While current applications demonstrate the feasibility of using feedback to promote improvements in kinematic measures such as joint ranges of motion, stride length, and walking speed [4] [5], as well as targeted muscle activations and spasticity [6],neuromuscular control feedback has yet to be considered. Recent research[7] suggests that quantifying subject-specific neuromuscular control is critical in improving intervention outcomes, therefore there exists a need to assess the effectiveness of integrating real-time motor control feedback into clinical practice.

The purpose of this study is to develop a system that uses electromyography (EMG) recordings to monitor muscle activity during dynamic tasks and generate patient-specific feedback on motor control complexity in near real-time. Currently, this system is being used to directly investigate the extent to which individuals can selectively alter their motor control in response to feedback and whether low-dimensional motor control metrics can be used effectively in feedback applications. Ultimately, this system will be used to provide insight into the efficacy of integrating motor control feedback techniques into clinical practice to aid clinicians in developing customized intervention plans that improve rehabilitation outcomes for individuals with CP.

II. METHODS

Custom Python script was developed to integrate all processes associated with time-synchronized data collection, signal filtering and data analysis, and data presentation via custom graphical user interface (GUI) in order to present motor control feedback to the user and update in near real-time.

A. Motor Control Calculations

Subject-specific motor control is calculated using muscle synergy analysis techniques. Muscle synergies, defined as weighted sets of muscles which typically activate together, are calculated using non-negative matrix factorization (NMF) [8]. Results from NMF analysis are used to calculate an individual's dynamic motor control index during walking (walk-DMC) [7]. Walk-DMC is a summary metric of synergy complexity that evaluates the total variance accounted for by a one-synergy solution, normalized to a z-score based upon average values from unimpaired walking. This score provides a convenient, low-dimensional assessment of motor control and, as such, is the feedback metric presented to users in this study.

III. RESULTS

The developed system is outlined in Figure 1. This system uses data streamed at 120 Hz from a 10-camera motion capture system (Qualisys), and a 16-channel EMG system (Delsys) to calculate motor control complexity as a user walks at a self-selected speed on an instrumented split-belt treadmill (Bertec).EMG data is streamed into the custom Python interface, filtered, and analyzed using muscle synergy

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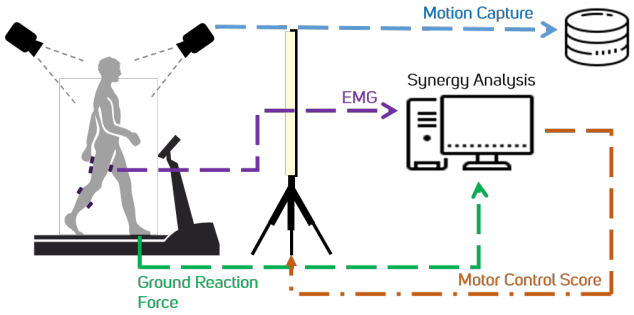

Fig. 1. An overview of the feedback system structure. EMG and ground reaction force data is used in real-time synergy analysis calculations to compute a motor control score. Motion capture data is stored for post-test analysis.

techniques. A one-synergy solution and the corresponding walk-DMC score is calculated for 10 concatenated steps [9], which are delineated using time-synchronized ground reaction force data taken from the treadmill. Near real-time analysis is achieved using a sliding 10-step window where, after a 10 step initiation period, walk-DMC is calculated with every newly identified step. The walk-DMC score for each window is displayed to the user via custom GUI. The GUI displays both a target walk-DMC score, set by the investigator, and a 15-score history to promote learning and maintain user motivation. Currently, the system latency is 0.1 seconds which allows users to see how changes in input directly affect GUI output and ensures that a wide variety of walking speeds can be tested without losing data due to system lag. Motion capture data is collected in parallel for post-test kinematic analysis.

The system facilitates experimental customization, as target walk-DMC scores, walking speed, the leg of interest, and the EMG sensors used can be modified before individual trials.

A. On-Going Trials

Currently, the system is undergoing verification testing using a typically developing pilot population to compare the accuracy and robustness of the algorithms against standard post-test synergy analysis. Upon completion of all verification activities, the system will be used to first analyze the extent to which an individual can selectively modulate their motor control score, as measured by their ability to achieve various walk-DMC target scores with and without feedback present. Data from these trials will be used to better understand the plasticity of motor control patterns as well as the extent to which individuals can respond to low-dimensional feedback.

The results from these preliminary investigations will be used to inform future system modifications, including alternative feedback metrics and methods. These results will also be useful in future studies with clinical populations where the viability of integrating real-time motor control feedback into rehabilitation for intervention planning will be assessed.

IV. CONCLUSION

To our knowledge, this study outlines the first instance of a system used to measure subject-specific motor control in real-time. Given the heterogeneity of the CP population and the importance of quantifying neuromuscular control in intervention planning, this system fills a critical need in rehabilitation. Overall, the system is a promising first step in investigating the extent to which motor control feedback can be incorporated into clinical environments to improve intervention outcomes and mobility for individuals with CP.

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Mechanical Design of a Novel Semi-Active Hybrid Unilateral Stance Control Knee Ankle Foot Orthosis

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***Abstract*—This extended abstract presents the first prototype of novel Stance Control Knee Ankle Foot Orthoses (SCKAFO) for support and facilitation of unilateral pathological human walking. The working principle of the orthosis and its main components are presented. The final system will be based on a novel controllable lower limb orthosis and its combination with non-invasive muscle electrostimulation.**

I. Introduction

THE incidence of Spinal Cord Injury (SCI) lies between 10.4 and 83 per million inhabitants [1] and 15 million people are affected by stroke annually worldwide [2]. Besides the physical impairment these neurological injuries cause, they also affect the quality of life of the person. Engineers and researchers develop assistive technology for rehabilitation and/or functional compensation of walking, aiming at enhancing quality of life.

Our goal in in the scope of the *Ibero-American Network for Rehabilitation and Assistance of Patients with Neurological Damage by Low Cost Robotic Exoskeletons* (REASISTE) project is to design a simple, affordable and efficient solution that supports neurologically injured patients' gait function. The proposed solution is based on the combination of Stance Control Knee Ankle Foot Orthoses (SCKAFO) with Functional Electrical Stimulation (FES), evoking a muscle contraction that is beneficial to the movement pattern. In this contribution, we present the mechanical design and working principle of the semi-active unilateral hybrid orthosis for the assistance and rehabilitation of pathological gait combined with non-invasive FES.

SCKAFOs constrain joint movement, providing stable support during standing and contributing to weight acceptance when they are locked. They can be classified according to the type of locking system (i. e. mechanisms with cables, bars and pawls that lock/unlock depending on the angular position of the joint, gravity and others [3]). Challenges to improve SCKAFOs are lighter designs, compact size and better performance of the locking/unlocking mechanisms.

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II. Matherial and Methods

The presented orthosis has 2 degrees of freedom and covers knee and ankle joints. It is designed to stabilize the knee joint during stance and enable assisted knee flexion and extension (completed by FES) during swing phase. FES also controls ankle dorsi/plantar-flexor muscles. Thus, the ankle joint in the orthosis is a simple passive pivot joint.

A. Working principle

The purely mechanical working principle of the device, combined with FES is explained in Fig. 1. In parallel, the muscles that produce dorsiflexion are stimulated and the ankle is planted to facilitate the phases of push off and swing during walking. The orthoses has a Bowden cable-driven locking system which blocks knee joint from stance phase until the beginning of knee flexion in the swing phase, where the locking system is deactivated and the knee joint can move free. Besides, the device has an elastic component that stores elastic energy during knee extension thanks to bi-articular muscular stimulation and gravitational forces. This energy is released and assists knee flexion during swing phase in parallel with the stimulation of the flexor muscles. When extension is completed, the locking system works again while the elastic component remains loaded until the knee flexion of the next gait cycle. Both systems are explained in more detail in the next two sub-sections.

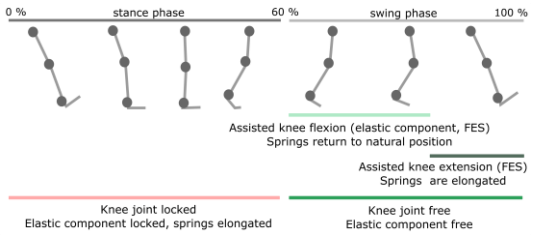

Fig. 1. Working principle of the orthosis, combined with FES, during a gait cycle.

B. Locking system

The locking system of the orthosis locks the knee joint during stance phase and release it during swing phase. The locking condition is the angular position of the hip joint. At the end of the stance phase, the non-affected leg supports user's weight. Suddenly, component A pushes component B of the mechanism located in the pelvis of the user. Then, component B moves vertically and Bowden cable pulls the spring deactivating the locking system. At the beginning of the next stance phase, with heel strike, the component C has

to push the component D in order to move it, compress the spring and activate again the locking system. The angular position of the component C can be regulated according to the desired knee locking angle (See Fig. 2).

C. Elastic component

The elastic component was designed and self-made for the orthosis. It is compounded by an inner and an outer ring. Both rings are connected by four linear springs (see Fig. 2). The outer ring is fixed to the upper bar of the structure while the inner one is fixed to the axis of the knee joint of the orthosis which is also fixed to the lower bar of the structure. Hence, the springs are elongated when a relative motion of these two rings is produced. Due to the locking system behaviour, the elastic component is blocked at the end of knee extension when the springs are elongated (see Fig. 1). The springs return to their natural length, delivering the stored energy, during knee flexion in the next gait cycle.

Torque to be delivered by the elastic component was calculated considering knee flexion acceleration and the inertia of the shank and the toe when performing knee flexion as a function of user's body weight [4]. Then, with known assistive torque at maximum deflection, we calculated the total spring stiffness, the maximum elongation of the springs and the force these should deliver to specify the elastic components. Besides, the elastic component's stiffness can be modified in order to be adaptable to different user's requirements. By manually varying the relative position of the rings before walking, the elongation on the springs can be increased which in turn increases assistive torque delivered by the mechanism.

III. Results

The presented orthosis is the first prototype developed in the scope of the REASISTE project. It is made of 3D printed pieces of PLA and weights 1 kg. Its principal components are a Bowden cable-driven locking system located at the pelvis level, a passive actuated knee joint with an elastic component that saves and releases energy and a simple pivot axis joint at the ankle level. The orthosis can be worn by users from 1.35 m to 1.95 m height and has two plastic braces with foam that adapt the orthosis to the user's leg comfortably. The orthosis will be attached to the pelvis of the user through a commercial hip orthosis. The structure also has hinges so that it follows user's leg shape in order to avoid joint misalignments between the user and the orthosis.

IV. Discussion

The design of the orthoses is simple because its working principle does not require sophisticated or complicated components. The prototype was made of 3D printed PLA in order to reduce the first manufacturing costs. However, with this material, the endurance of some of the pieces is compromised. For example, the axis of the knee joint was manufactured in steel. Thus, in order to maintain affordability and lightness, only the most compromised pieces when supporting internal forces developed in the orthosis should be manufactured in aluminium.

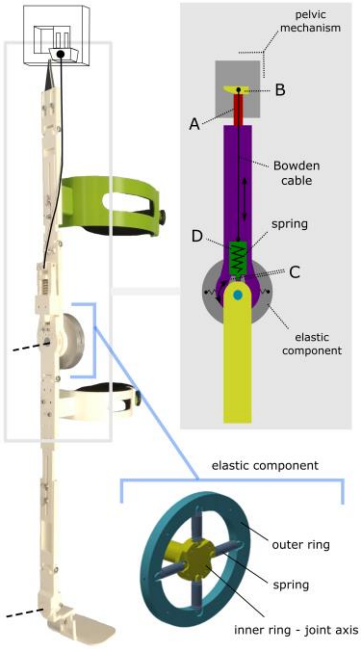

Fig. 2. First prototype of the orthosis and conceptual scheme with its principal components.

V. Conclusion

The first prototype presented is a light design and has a compact size. The orthosis support the weight of the user during the stance phase while allows knee joint free movement during swing phase. Thus, the locking/unlocking system works properly. Next steps will be verifying the amount of energy delivered by the elastic components, manufacturing pieces that support high efforts in aluminum and testing the orthosis in combination with FES to prove its efficiency.

Acknowledgment

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Quantification of deficits in motor planning in cerebral palsy

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Abstract— **Children with cerebral palsy (CP) exhibit deficits in motor planning during upper-extremity tasks that affect the efficacy of their movements in everyday life. Although clinical studies have demonstrated that these deficits exist, it is challenging to quantify these deficits, and it is unclear to what extent motion planning plays a role in movement impairments associated with CP. Control theory provides new methods to quantify and assess motor planning strategies. By monitoring an individual's performance during specified movements, such as a trajectory tracking task, we can model the role of feedforward control (i.e., reflecting motor planning) and feedback control (i.e., error correction) during movement execution. Quantifying impairments in motor planning for children with CP and evaluating their relationship with standard functional tests will help illuminate the mechanisms underlying impaired movement in CP and inform treatment planning.**

I. INTRODUCTION

CEREBRAL palsy (CP) is a neurological disorder caused by brain injury or anomalies during neural development. It affects 2-2.5/1000 live births [1], and mainly causes impairment of motor function [2]. While most clinical studies and rehabilitation for children with CP focus on motor execution, recent studies have shown that impaired motor planning may be just as limiting for the performance of daily activities [3], [4].

Motor planning is the ability to integrate sensorimotor information to plan an action ahead of execution. It is a skill that is acquired as an individual encounters novel scenarios and environments during development. Traditional motor planning experiments test whether children plan their movements to end in a comfortable posture, or whether they instead use a step-by-step strategy to perform upper-extremity tasks [4]. An example of a such an experiment is the act of picking up a cup that is upside down so an individual can drink out of the cup. Unimpaired individuals will pick up the cup with an uncomfortable underhand grip so that when the cup is flipped over, the ending grip will be a comfortable overhand grip for drinking, while individuals with impaired motor planning will start with a comfortable overhand grip, and will have to readjust their grip before using the cup. Although this experimental design allows researchers to elicit deficits in motor planning, it cannot quantify the extent of the deficit in motor planning skills. With this experimental paradigm, prior research has demonstrated that unimpaired children are able to plan ahead to end in a comfortable position as they age and gain experience [5]. However, when children with CP are tasked with this experiment, they prefer a comfortable starting grip regardless of age, indicating a step-by-step planning rather than anticipatory motor planning [3], [4], [6].

Upper-extremity functional tests are also commonly used to assess motor function. However, it is difficult to attribute motor deficits quantified in these functional tests to motor planning deficits or other physical impairments. Differentiating motor planning and motor execution will be invaluable for quantifying planning deficits and designing personalized interventions. There are multiple theories as to why children with CP have difficulty forward planning compared to unimpaired children. First, children with CP are believed to lack experience with motor planning due to increased aid from parents as compared to unimpaired children [7]. Second, there may be a decreased ability to imagine a movement without performing it (motor imagery), leading to difficulty planning ahead to perform motor tasks [3], [4], [6], [7], [8]. In children with hemiplegic CP, those with damage to the left hemisphere had difficulty planning ahead and with motor imagery, which impacted their performance of daily activities [3]. Neuroimaging studies demonstrated that motion planning requires recruitment and coordination of distributed neural networks in the left cerebral hemisphere including the frontal and post-parietal cortex [9], [10]. Research on monkeys involving preparation of movement revealed that motion planning requires interactions between the post-parietal cortex and the frontal motor cortex [11], which are affected in CP. However, it is unclear to what extent children with CP are affected by deficits in motor planning compared to unimpaired children, as the current experimental design makes it difficult to differentiate between the physical impairment and motor planning deficits. Quantifying the degree of motor planning impairment would enable new clinical tests to assess and individualize rehabilitative interventions to improve motor planning.

II. METHODS

A. Computer Task

Following a procedure developed in [12], [16], a trajectory tracking computer task was created in Python2.6 using Pygames, such that the player follows a yellow trajectory

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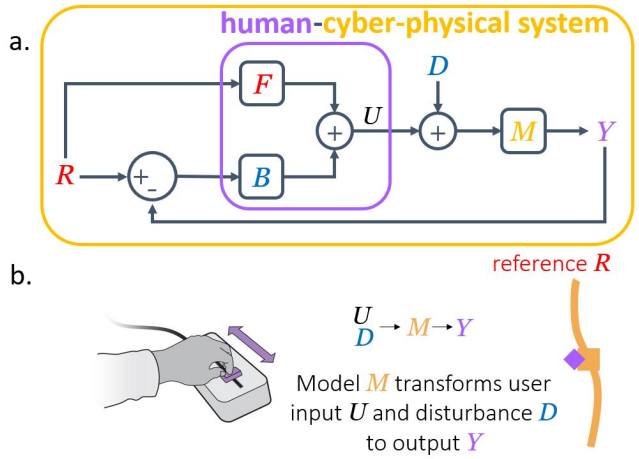

Fig. 1. a. The block diagram of HCPS highlights the feedback and feedforward human controller separation that combines to a measured user input U. Our experimental assays prescribe the reference and disturbance signals, r and d, as well as the cyber-physical model, M, and are designed to enable estimation of the distinct contributions of feedforward and feedback processes. b. A human operator completing the computer trajectory tracking task using a 1DOF slider.

using a purple cursor. A one-degree of freedom (1-DOF) slider was developed using a potentiometer attached to an Arduino Due, and a comfortable joystick was 3D printed (Fig. 1b). Reference trajectory and disturbance rejections (applied to the user as an invisible force to their input) were generated as a phase-shifted sum-of-sines, with interleaved frequencies at prime numbers from 2-31 inclusive with a base frequency of 0.02 Hz.

B. Data Collection

Ten unimpaired individuals will be recruited to participate in the study. After going through a series of trials to test their reaction time, they will go through 40 trajectory tracking trials, with each trial being 45 seconds long. Individuals will be instructed to minimize the distance between their cursor and the yellow reference trajectory, and to minimize their "score", a modified mean-squared-error, which was displayed on the screen at the end of each trial. A first-order plant will be used to transform the user input into the cursor output.

A similar protocol will be followed for one individual with cerebral palsy (MACS Level), and they will also asked about their level of impairment.

C. Separation of Feedforward and Feedback Controllers

Previous work demonstrated that the human sensorimotor controller is comprised of parallel feedforward and feedback pathways, F and B respectively (Fig. 1a). The dynamic inverse model mathematical framework [12] suggests that humans learn the forward model M and implement the inverse model as a feedforward controller, $F = M^{-1}$.

All data will be analyzed in the frequency domain. Feedforward and feedback contributions to the trajectory tracking task were separated in the frequency domain by computing the transfer functions H_{UR} and H_{UD}, which map the reference and disturbance signals, respectively, to the user input.

We may express these empirical transforms as functions of the unknown feedforward and feedback controllers, F and B:

$$U = \underbrace{\frac{F+B}{1+BM}}_{H_{ur}} R + \underbrace{\frac{-BM}{1+BM}}_{H_{ud}} D, \tag{1}$$

$$Y = (U+D)M. \tag{2}$$

Or conversely, we estimate the feedforward and feedback controllers as functions of the empirical transforms and the prescribed system model:

$$B = \frac{-H_{ud}}{M(1+H_{ud})}, \tag{3}$$

$$F = \frac{H_{ur} + M^{-1}H_{ud}}{1+H_{ud}}. \tag{4}$$

D. Data Analysis

The mean-squared error between the feedforward controller and M^{-1} will be used as a metric to assess motor planning. If the subjects are able to learn the dynamics of the model that transforms their user input into a cursor output and sufficiently plan ahead, their feedforward controller should be similar to M^{-1}.

III. Conclusion

This paper presents a novel method to assess motor planning and learning in individuals with cerebral palsy. We plan to implement this protocol this summer to quantify motor planning and learning in unimpaired individuals and individuals with cerebral palsy. We expect to have results of our study by fall, 2018. The conclusions of our study will aid in more targeted and individualized treatment planning for individuals with cerebral palsy.

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A review of human locomotion databases: preliminary results

D. Pinto-Fernandez, D. Torricelli and J.L. Pons

***Abstract*— This paper reports a preliminary overview on the existing datasets and databases of human locomotion. This analysis was conducted to identify the existing databases in this field, their main goal and structure, as well as to collect information about the necessities, preferences and deficiencies on this topic within the scientific community. Based on this results, we aim to stablish a robust design criteria for developing the first human-wearable-robot locomotion database.**

I. Introduction

ASSESSING the performance of wearable robots is a necessary step to demonstrate the ability of research prototypes to work out of the lab and meet users' expectations and needs [1]. The European project Eurobench will establish the first European robotic framework for bipedal locomotion benchmarking and will provide the robotic community two facilities with this purpose.

This is a great opportunity to collect data from lots of robotic devices. This data should be uploaded and organized in a database where the scientific community could access, download and upload their own data with a specified format and structure.

The first step in this direction is to understand the state of the art on this topic. We performed an extensive review of the literature, focused on the following questions: "How many locomotion databases are available?", "What does each database contain?" and "How are these type of databases currently structured?". In this paper we report the preliminary results of this analysis and discuss the main relevant findings emerged so far.

II. Material and Methods

We performed an initial search on the Scopus scientific database using the following query string on paper title: ((gait* OR locomot* OR walk*) AND (database* OR dataset*)). The resulting 79 publications were filtered by reading titles and abstracts, looking for the presence of actual and available databases. We excluded publications that were not related to the definition or usage of any database of that kind. With this first search query, we couldn't find any robotic locomotion database, so, to the resulting 44 papers we added 6 publications resulting from a further search query aimed to find papers covering robotic locomotion databases: ((gait* OR locomot* OR walk*) AND (TITLE (database*OR dataset*) AND (robot* OR "wearable robot*". OR exoskelet* OR humanoid* OR "powered orthos*")).

These 50 publications were further analyzed focusing on two main aspects: The presence of state of the art databases and the definition and creation of databases' structures.

III. Results

At Table 1 preliminary results of the search are shown. We found 20 databases. Five of them were divided in datasets or sub-databases with different goal or content.

We found four different categories for classification. Gait recognition and biometric databases represent 45% of the existing databases. Another 45% of the state of the art databases are gait analysis and biometric data ones. We found another 20% of gesture and action analysis and recognition and only one out of 20 (5%) contained clinical data.

TABLE I
List of Databases Found and Goals

Day	Database Goal	Reference
CMU Mobo	Gait Recognition	[2]
SOTON	Gait Recognition	[3]
CASIA-GD	Gait Recognition	[4]
CASIA-AD	Gait Recognition	[5]
AVA Multi-View	Gait Recognition	[6]
KY 4D	Gait Recognition	[7]
OU-ISIR	Gait Recognition and Analysis	[8]
HuGaDB	Gait Analysis	[9]
Daphnet	Parkinson's Gait Analysis	[10]
USF	Gait Recognition	[11]
MAREA	Locomotion and gesture recognition	[12]
GRACE	Locomotion and gesture recognition	[13]
TST-Fall	Fall Detection	[14]
Mocap	Gait Analysis	[15]
CMU-GLMCD	Gait Analysis	[16]
ISB	Gait Analysis	[17]
HuMoD	Gait Analysis	[18]
HOOD	Gait and Action Analysis	[19]
HIDGC	Gait Recognition	[20]
SRLAB	Clinical data	[21]

IV. Discussion

All the gait recognition and biometric databases contain

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images or video, and the most common files are .png and .avi. A lot of this biometric databases have also pre-processed data containing gait models and subject silhouettes.

Srlab, which is a huge database containing clinical data, and the Daphnet database which analyses Parkinson's disease gait are the only ones we found involving patients. The other 18 databases contained only healthy subjects' data.

We didn't find a common structure at these databases. The only common point is that the majority require an agreement and an acknowledgement of the terms of use signed to be accessed, which is very important for controlling the usage of the data.

It is usually required extra software to decrypt or process the data contained at the datasets. The most requested software is Matlab and .C3D viewers for motion capture datasets. In terms of Data acquisition, the preferred method found is photogrammetry, but some marker based motion capture and IMU based databases have been found.

V. Conclusions and Future Work

We provided here some preliminary results on a currently ongoing review work on the state of the art of the human locomotion and gait databases. This overview was conducted to identify existing databases and its main categories.

We identified two main goals: gait analysis and recognition. We found interesting that only two of these databases contain clinical and patients' data. Another interesting finding was that there is no availability for robotic locomotion datasets, which we consider very important for the evolution of the state of the art technologies.

As future work we propose to continue developing this review to identify the existing database's structures, as well as to collect information about the necessities, preferences and deficiencies on this topic within the scientific community. Based on this results, we aim to stablish a robust design criteria for developing our own database at Eurobench.

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Proposal of a Stackable Functional Electrical Stimulation System Device

C. Rodrigues, A. Ortiz, J. C. Moreno and J. L. Pons

Abstract— **Functional Electrical Stimulation (FES) is a technique that applies electrical pulses to impaired or paralyzed muscles to restore or improve their functions. Methods that make use of FES systems are being increasingly used in clinical rehabilitation and research to produce muscle contractions from electrical stimuli. The applications of FES devices go to drop foot inability to restoration of upper and lower limb in spinal cord injures patients. This paper presents a proposal of a stackable one-channel surface FES system device. The based concept of the device is to develop an one-channel stimulator that can be liked with others using a communication potocol, where the messages are send by a control unit. This design makes it possible to provide a FES device with variable output channels, being all indepent between each other, what leads to a more flexible and personal system to the user's purpose and needs.**

I. INTRODUCTION

NeuroMuscular Electrical Stimulation (NMES) can be defined as the application of electrical pulses to motor points in order to artificially contract skeletal muscles [1]. The Functional Electrical Stimulation (FES) term was patented by Moe and Post in 1967 as an "Electrical stimulation of muscle deprived of nervous control with a view of providing muscular contraction and producing a functionally useful moment" [2]. FES can, therefore, be defined as a technique that applies electrical pulses to paralyzed muscles to restore or improve their function [3], better saying, the application of NMES to supplement or replace function that is lost in neurologically impaired individuals [4].

The method of electrical stimulation was primarily used by Liberson et al. [5] in 1961 to restore the peroneal nerve of hemiplegic patients suffering from drop foot [1]. Since then, the method of electrical stimulation has been used in different areas such as preventing bladder and bowel incontinence, reducing spasticity, regulating heart rhythm and improving paralyzed limbs [4], [6]–[9].

Due to the increasing use of FES methods, several FES devices are being developed and researched.

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Breen et al. developed a 2-channel programmable and portable stimulator with algorithms for drop foot correction as well for blood flow assist [10].

Popovic et al. built the Compex Motion stimulator, wich presents four current regulated stimulation channels and has two input channels that can be configured as analog or digital input channels, besides that, this stimulator can work with a parallel configuration of stimulator device, expanding the number of stimulation channels in multiples of four [11].

The objective of EXTEND is to develop all the necessary tools to achieve a minimally invasive bidirectional neural interface platform capable of distributed stimulation and sensing of neuromuscular activity, for attaining what we refer to as Bidirectional Hyper-connected Neural System, BHNS.

This network will create novel channels of communications between various sensory and motor nerves, providing the means of a synthetic chain of action-reaction of sensorimotor activity.

EXTEND will develop the technology for Bidirectional Hyper-connected Neural Systems (BHNS), these systems will allow the connection between a network of implanted wireless stimulators/sensors and external devices and tools [12]. The proposed FES system will be, therefore, used in the earlies stages of the EXTEND project, providing a net of superficial FES stimulators that can be used before the final inserted implants.

The concept to the design of the system here proposed is, thus, carried out to attend the needs of said project. Finally, is going to be develop an one-channel surface stimulator that can be linked with others by a communication protocol, here is proposed the CAN communication, controlled by a control unit. This design makes it possible to provide a FES device with variable output channels, beeing all indepent between each other. This design makes this FES system device more flexible and personal to the user's purpose and needs.

II. MATERIAL AND METHODS

The FES stimulator proposed in this article can be seen as a stackable block device, where a block can be interpreted as a single-channel stimulator device.

The stimulators devices are going to be controlled by a master block, or control unit. This block will be responsable of sending the stimulation parameters to the simulators.

The communication between the control unit and the stimulators is going to be performed by a CAN communication protocol. This communication protocol is based on a distributed scheme, where there's a central unit, allowing a direct data transfer between any two or more nodes without a master mediation [13].

In Figure 1 is shown a diagram of the proposed system, where we can see the control unit linked by the CAN protocol to the single-channel FES devices.

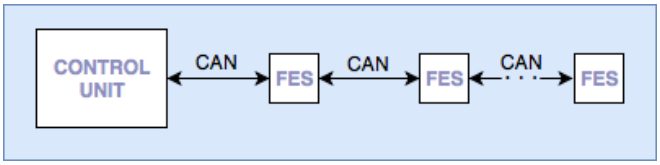

Fig. 1. Schematic of the proposed system. The control unit is the master block wich is linked to the other blocks, responsible for the functional electrical stimulation. The messages between blocks are going to be send by a CAN protocol.

The FES system proposed in this article is planned to allow more flexibility to the user, that is possible once, with one control unit, the user can attach several single-channel FES stimulators. The maximum quantity of stimulators is going to be limited by the number of messages existing in the CAN protocol and the control's unit processing power.

III. Discussion

The arrangement of the FES system presented, in stackable blocks can provide some important advantages:

- Flexibility: the final FES device here proposed do not have a fixed number of channels, this feature is defined by the user's need. This characteristic leads to a personal assembly to each case and patient.
- Not demultiplexing output: Several FES devices, to have more outputs options, make use of demultiplex one stimulation signal in several ones. This method can lead to delays in the device's output. The FES system here proposed don't need to make use of such action, once present a simple direct output signal.
- Independent channels: unlike most of the current stimulators, this proposal provides the possibility of having an all independent channel stimulator, that means, each stimulation signal output will have its proper ground. This characteristic allows local and independent muscle stimulation, avoing also galvanic burn.

IV. Conclusion

The FES technique is progressively being used in clinical rehabilitation and research to produce muscle contractions from electrical stimuli. The applications of FES are being increasingly used, which leads to more researches and creation of functional electrical stimulator devices.

The FES stimulator device here proposed have a different concept from the stimulators being used in this moment. Its disposition provides flexibility, independency between its channels and facility of use, making this proposal promising in the FES devices developing area.

The arrangement of this stimulator allows future implementation of EMG signal sensor in each independent block, using the CAN communication as well to send parameters and read EMG signals.

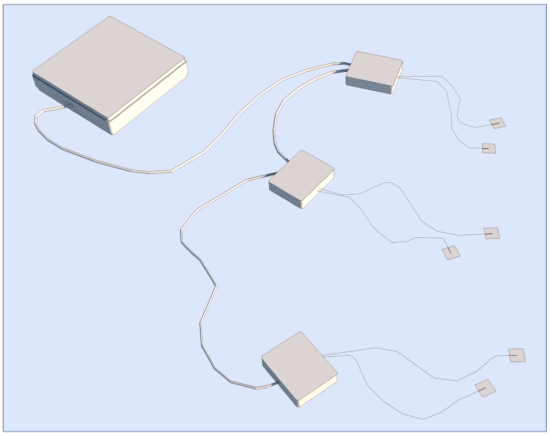

Fig. 2. Proposed design of the FES system. A control unit linked to three single-channel stimulators.

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The Need for Studying the Biocompatibility and Safety of Biomimetic eAXON Neuro-prosthetic Systems

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***Abstract*—Minimally invasive wireless addressable single-channel micro-stimulators called the eAXONs (for electronic axons) will be injected intramuscularly to excite paralyzed muscles that have lost their neural drive due to trauma or stroke. The eAXONs will deliver stimulation through electronic rectification of innocuous high frequency currents applied through epidermal electrodes. This innovative stimulation method pushes the limit of miniaturization to the point that the diameter of the eAXONs will be only a fraction of that belonging to the thinnest microstimulator attainable by current technologies. Due to the high level of miniaturization, we envision the implantation of a large density of eAXONs per muscle to improve control over muscle activation and reduce fatigue. It is known that the implantation of intramuscular devices can induce muscle damage. However, the relationship governing the number of devices and extent of muscle damage remains unclear. Moreover, the effect of electrode separation distance on the biological tissue response produced by intramuscular devices has never been investigated. Both have important implications on the safety, in vivo performance and clinical translatability of the eAXON neuro-prosthetic systems.**

I. Introduction

Patients who suffer from paralysis more often than not have intact peripheral motor nerves that can be artificially excited to effect functional movement. Functional electrical stimulation (FES) is the application of low stimulation currents to lower motor nerves to restore movement to paralyzed muscles. Current fully implantable FES systems consist of several stimulating electrodes whose conducting leads are routed subcutaneously and connected with an internal stimulator placed remotely in the chest or abdomen area[1]. Such wired FES systems are composed of bulky hardware whose implantation requires invasive surgeries. Moreover, the leads cause a reliability problem due their vulnerability to fracture and migration during evoked muscle contractions[2]. Contrarily, implantable wireless FES systems consisting of independent single-channel stimulators have the advantages of low invasiveness and high durability due to the elimination of leads. An example of such system is the BIOnic Neuron or BIONs developed by G. Loeb et al.[3]. The BION is a cylindrical micro-stimulator that is thin enough (2 mm in diameter) to be implanted by injection into the muscle via a hypodermic needle in a minimally invasive technique. With this system, multi-site stimulation can be accomplished by combining several channels or BIONs forming a network to re-innervate a large area of the body.

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II. Electrode density in FES

Conventionally, FES is applied to a single point in the muscle. Such low electrode density is accompanied by early muscle fatigue and unstable recruitment[4]. Furthermore, it was demonstrated that there is a direct correlation between the number of stimulation channels and the level of control and complexity of artificially produced movements[5]. Nowadays, the implantable wired FES systems are only available in 8 or 16 stimulus-channel configurations. The BION system can support up to 256 channels, yet the relatively bulky size and rigid design restricts their implantation in large numbers. Challenging the current limit of electronic miniaturization can bring about the development of extremely thin devices. Subsequently, this would open up the possibility of implanting a large number of devices inside the muscle to control it without causing excessive muscle tissue damage. A motor prosthesis based on a low number of stimulation channels falls short of emulating the natural mechanisms of muscle activation resulting in quickly fatiguing and poorly controlled muscle movements. However, in the case of the eAXON system, fatigue resistance and motor control are improved by placing a large number of eAXONs. Such high innervation density is similar to that naturally found in the muscle and thus eAXON system embodies a biomimetic control method capable of producing movement similar to that generated by volition.

There is another advantage to having a large number of stimulus channels. In FES, it is known that high stimulation frequencies are linked to early muscle fatigue. The presence of several channels allows stimulation to be delivered at a lower frequency than would be possible with a single channel and thus fatigue can be delayed[6]. However, the use of low stimulation frequency gives rise to tremors due to the incomplete fusion of the individual muscle twitches. The existence of many channels provides a window to perform interleaved stimulation. Interleaved stimulation refers to implementing a time delay between stimulation of different channels to obtain smooth contractions while retaining fatigue resistance associated with low frequency stimulation.

III. The eAXON project

The eAXON project focuses on the development of an

extremely thin and flexible wireless neuromuscular interface aimed to be injected into the muscle[7]. Each eAXON can be activated independently of one another through a specific address. Fig. 1 shows a non-addressable prototype of the eAXON. Compliant materials (mainly silicone) will be used in the construction of the eAXONs. The flexibility of the eAXONs will act as a stress relief mechanism which will minimize tissue damage caused by friction during muscle movement. The eAXONs receive power and stimulation commands wirelessly from an external generator using galvanic coupling through rectification of high frequency bursts. This method of implant powering does not require bulky components like coils or batteries leading to an unprecedented reduction in implant size. The fact that the eAXONs enjoy a high level of miniaturization, leads to the possibility that many of them can be implanted in a single muscle to biomimetically control its contraction.

Fig. 1. Picture of the current eAXON prototype (⌀ 1 mm)

IV. SAFETY & FOREIGN BODY RESPONSE

Perhaps the most unconventional aspect of the eAXON technology is that the injection of a large number of devices in muscles is required. This represents a paradigm shift from the standard techniques applied in FES practice that are based on small interface density. The implantation of a large number of stimulators was not previously attempted due to size constraints imposed by the lack of appropriate miniaturization technologies. An important step towards demonstrating the potential of the eAXON technology to be used in humans is to evaluate its safety and efficacy using animal studies. It is unknown if the presence of the eAXONs will cause significant muscle damage and if this damage will be dependent on the number of implanted devices. Moreover, there are uncertainties concerning the anchorage behavior of the eAXONs inside muscles. Ironically, muscle movement caused by activation of the eAXONs renders them susceptible to migration and subsequent failure.

Foreign body response or FBR corresponds to the sequence of acute and chronic immune-related events that unravel subsequent to implantation of a medical device. The immune response culminates in the formation of a collagen capsule that isolates the device from the excitable tissue. The increase in the physical separation and electrical impedance between the eAXON and the target tissue caused by the collagen capsule may lead to partial or complete loss of efficacy. Adequate in vivo functionality of the eAXONs can be ensured when the fibrotic capsule is kept as thin as possible. There are several factors that aggravate the FBR including mechanical factors. The number of implanted eAXONs per muscle and their separation distance may indirectly influence the thickness of the FBR by re-distributing the stresses inside the muscle. Large number of eAXONs placed at small inter-electrode distances may cause the accumulation of stresses near the eAXONs leading to excessive mechanical trauma. Ultimately, these changes can exacerbate the FBR and result in device failure.

V. CONCLUSION

The eAXON neuroprosthetic system independently recruits sections of muscles rather than whole muscles to effect movement of paralyzed limbs. The eAXON approach may hold the key to unlocking the problems of fatigue and unrefined movement control which have stifled the clinical success of FES for decades. However, stringent evaluation of the safety and efficacy of the eAXON technology still needs to be conducted.

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Survey of Common Issues in Magnetic Inertial Sensors: Main Neuro-Rehabilitation Applications

E. A. Belalcazar-Bolaños, J. O. Roa-Romero, and J. L. Pons-Rovira

Abstract— **The development of interactive neuro-rehabilitation technologies based on motion tracking has attracted attention from several research fields. In particular, Magnetic Inertial Measurements Units (MIMU) has been widely studied in the latter years as it is a cost-effective enabling technology for those applications in which motion tracking based on optical technologies is unsuitable. A methodology for a systematic survey of MIMU sensors in neuro-rehabilitation applications and their common issues in human motion capture systems is presented. Results shows several applications in neuro-rehabilitation and the main challenges that IMU sensors must address.**

I. Background

Due to the growing population, in the past few decades, many health-care problems have highlighted. According to the World Health Organization, currently 15% of people suffer from musculoskeletal disabilities; among these 15%, 35%-50% of disabled people in modern countries are not getting the necessary management: diagnosis, treatment, follow-up. This number is even higher in developing countries and reaches 76%-85% [1]. To recover any dysfunction of body locomotion, and to improve surgical outcomes of musculoskeletal patients, functional rehabilitation is one of the most efficient routine. Usually, a rehabilitation program is assigned by a clinical expert to a specific patient, and then the execution and follow-up are managed by a therapists team. The direct therapist intervention presents some limitations that require therapists to always follow, guide, and physically support their patients [2]; So, a significant number of therapists is required to ensure the quality of the rehabilitation program. This fact led to establish a research field as a complementary tool for therapeutic sessions, with an objective evaluation of the rehabilitation process.

In this field a large range of sensors such as Microsoft Kinect, Wii Mote, Wii Fit, force plates, and Magnetic Inertial Measurement Units (MIMU) have been used as interactive tools between the subject and the virtual environment of the developed systems [3]–[5]. The most commonly sensor used is the Microsoft Kinect, due to its low price and big success with Xbox games. Furthermore, in order to use these visual or inertial sensors for body tracking in serious games, the sensor needs to be able to estimate the orientation of any considered limb and the respectively joint angles [4]. Traditionally, the universal goniometer was the most famous tool for joint angle estimation, and more recently the motion capture system based on photometry is commonly used for the same propose. However, even though these two tools are considered as the golden standards for orientation angle estimation, they are neither portable nor cost efficient. This lead to a growing interest in using MIMU system in particular.

The main applications related to MIMU sensors include walking speed estimation [6], gait analysis [7], pedestrian dead-reckoning [8], activity classification [9], rehabilitation, ergonomic, etc. Typically, 9 degrees of freedom (9DOF) are considered by means of tri-axial acceleromenter, tri-axial gyroscope, and tri-axial magnetometer. By taking into account some conditions such as homogeneous magnetic field, the attitude and heading can be estimated from gravitation acceleration and geomagnetic field, respectively. Meanwhile the attitude and heading updating is carried out by the integration of gyroscope measurements. However, there are some limitations when the sensors are considered separately; acceleration caused by motion, gyro integration drifts, and magnetic distortions [10]. Thus, sensor fusion is required for compensating errors and improving orientation estimation accuracy [11]–[13].

Due to several applications in neuro-rehabilitation consider the use of MIMU sensors, this article present a methodology for a systematic survey of neuro-rehabilitation applications and common issues in human motion capture systems; both focus on MIMU sensors. In section II is described the process considered for the systematic survey and section III show the main literature selected. Finally, section IV present the main conclusions about the survey.

II. Method

A. Literature search strategy

The four main databases for both engineering and health applications were taken into account: ACM, IEEE Xplore, PubMed, and Scopus. Papers addressing the following aspects were selected: rehabilitation, MIMU, drift, constraints, magnetic disturbances. Title, abstract, keywords and their spelling variations and synonyms were considered in each database. Articles published from 2004 to 2017 were included. This search includes refereed journal papers and peer reviewed articles published in conference proceedings. Only English articles are included.

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B. Study selection process

The PRISMA [5] guidelines were considered in the following steps for article selection process:

1) A manual search strategy was performed since 2018 on each database.
2) After removal duplicates, it was screened titles and abstract of remaining articles
3) Full texts were read and then selected articles based on the inclusion/exclusion criteria.
   Inclusion criteria were: a) Neuro-rehabilitation purposes, b) Upper, lower and full body, c) Main issues in MIMU systems, d) Magnetic disturbances, e) Biomechanical constraints, e) bias and drift, f) Articles were written in English.
   Exclusion criteria: Sensor fusion with MIMU and other technology.

C. Data extraction process

The extracted data included the technology used in applications in neuro-rehabilitation, kinematic constraints, drift, and magnetic disturbances.

III. Results

A. Applications in Neuro-rehabilitation

In the last decade several researchers have focused on the development of portable, cost efficient, and reliable tools based on MIMU sensors. Some studies had following aims: improve active joint range of motion, improve movement performance, improve movement coordination, improve posture, improve muscle strength, overcome learned non-use and improve performance of activities of daily living skills. In [14]–[23] **Stroke** rehabilitation is considered, by using of MIMU sensors in process such as body segment posture, improve posture and movement performance. Besides, [24] depicts a rehabilitation process in **Spinal Cord Injury** considering body segment posture, and improve moment performance. The same techniques are applied in neuro-rehabilitation in children with **Cerebral Palsy** [25].

One of the most common application of MIMU sensors is gait analysis, for diagnosis or treatment aims. In recent years **Parkinson** and **Alzheimer** disease have attracted the attention of the scientific community in topics such as detection of the pathology and estimate the stage. In [26], [27], the authors use MIMU sensors in lower body for a early detection in both diseases.Although they are neurodegenerative diseases, therapies allow to reduce the speed of degeneration of the pathology.

B. MIMU issues

Common issues in human motion capture systems based on inertial measures are considered and the main strategies to deal with. Following, main issues due to the sensors and environment interaction will be presented.

Kinematic constraints (KC) The fundamental role is to prevent the relative displacement of the body segments to drifts over time. Typically, KC could be embedded in the sensor fusion algorithm to provide more consistent solution, or after when the attitude estimation is provided [28]–[31]. In [28]–[30], [32]–[35], the elbow is constrained to reduced DoFs. In contrast to the kinematic chain model, free segments models have been proposed [31], [36]; these anatomical constraints representations consider hard constraint, e.g., the connectivity between successive limbs [36], while the soft constraints are relaxed in order to reduce the effects of errors related to their implementations. **Drift** A solution based on integration of gyroscope is adapted to follow the human motion dynamic, but it cannot be used alone because the estimation quickly drifts. A common solution for reducing drifts is fusing Inertial Navigation System (INS) with a quasi-static one, as it develops in many complementary filters approaches [12], [37]–[40]. Another solution considers constraints from kinematic chain to avoid drifting attitude estimate of one limb with respect to the others [28]–[30], [33], [34], [39], [41]–[45]. A further solution used mainly in lower limbs tracking and exploiting contacts of the feet with the ground [39]. When the foot is in contact with the ground its velocity is almost null. This information can be used to reset the speed, this method is commonly known as zero velocity update (ZVUT). These techniques have highly reduced drifts as showed in several studies.

Magnetic disturbances The most accurate methods consider the magnetometer signal for attitude estimation and drift correction. However, this signal are easily distorted by the presence of ferromagnetic materials. Typically, distortion effects are classified as hard and soft iron interference [11], [46]; hard iron effects causes an offset of the earth magnetic field whereas soft iron effects causes a distortion. If the magnetic environment does not change, these effects can be corrected through internal sensor calibration. On the other hand magnetic fields variations of space and time is a dealing task (no-homogeneous magnetic field). The simplest solution is to establish a decision criterion when magnetometer signal is reliable. This can be done by thresholding its magnitude [47], [48]. Another common solution is limiting the contribution of the magnetometer measurement to the heading variable [28] or two components [12]. Moreover, a novel solution suggest a model-based estimation of the disturbance, in [49] the authors consider that the magnetic field direction is estimated simultaneously with the sensor orientation.

IV. Conclusions

A robust methodology was presented for a systematic survey of neuro-rehabilitation application using MIMU sensors; moreover, it is considers their common issues in human motion capture system. The method proposed allows to discard redundant information, to find a set of diseases where neuro-rehabilitation has been used with the sensors, and to limit the main challenges that must be solved for a correct measurement in MIMU sensors.

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Assessing Safety and Performance Indicators in Rehabilitation Robotics

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***Abstract*— Healthcare is one of many domains where robots interacting with humans are becoming increasingly relevant. New technologies are being developed but the deployment in rehabilitation is restricted by a lack of unified testing methodologies. The two European projects COVR and EUROBENCH are working to break down those barriers. The goal of this contribution is to provide an overview of both projects and how they will contribute to a unified testing methodology for safety and benchmarking.**

I. Introduction

ROBOTIC technologies in rehabilitation are developing rapidly. An ageing population and a shortage of skilled clinicians increase the need for robotic devices which can ensure positive rehabilitation outcomes and at the same time lighten the burden of clinicians' work. Rehabilitation robots can provide high intensity and dosage training which were found to be key therapeutic modalities for the improvement of functioning in daily living. [1] Moreover, they can assist and guide movements in patients suffering from motor impairments and can assess the patient's motor capabilities [2].

Although rehabilitation robotics is a very promising and fast developing field, there are a number of barriers in the process of moving applications out of the lab and into everyday applications. Some of these barriers are technical while others are related to a lack of reliable indicators for performance and safety. Robotic systems used in healthcare have to be safe and take the clinical needs of patients into account. This can be a major challenge since there often is physical interaction between the user and the robot and there is a lack of recommendations for the safety testing of those physical interactions. In addition to that, comparison of the performance of different robotic systems is desirable as it can give insights on what robotic system is most used for what category of patients. Therefore, benchmarking is also an important endeavor to pursue. Rehabilitation robotics is by default a multidisciplinary field [3]: Care practices and technology developers need to work hand in hand to allow for innovative ideas to meet patient requirements and be accepted for use based on successful clinical trials.

In order to overcome these barriers and push technologies to market, there is a need for evaluating both performance and safety of robotic systems in real-life environments. Methodologies for benchmarking and safety evaluation are needed not only for rehabilitation robotics but for all robots interacting with humans.

Two European projects which share the aim of pushing new technologies to market by providing methodologies for assessing robot skills/abilities have recently been launched. The concepts of those two projects will be explained in the following section.

II. Concepts

A. COVR

The mission of Horizon 2020 project COVR (*Being safe around collaborative robots*; www.safearoundrobots.com) is to significantly increase the safety of collaborative robots which are all robots working in shared spaces with humans. Unless safety regulations become easy to access, understand and apply, it can become a barrier to the increased deployment of collaborative robots that industries across many domains demand. Therefore, five national research and technology organizations are working together to offer a single-point-of-access framework for validating collaborative robot safety, organized around EU directives and standards, accessible to everyone.

One fundamental part of this framework will be a toolkit which can help identify relevant safety testing protocols for physical human-robot interaction scenarios. It will identify the standards that are relevant to any type of collaborative robot by asking a series of questions. The output includes checklists of skill-based requirements that need to be fulfilled, and instructions for performing validation tests.

In many cases, the relevant standards do not clearly define the safety-related validation procedures in sufficient detail. Wherever this is the case, COVR uses experience on best practice and cross-fertilization among sectors to fill the gaps. For instance, if the standards for medical electrical equipment do not specify validation procedures or pass values for the identified item, information from industrial experience can be used. An important aspect of the development of new testing protocols is an active consultation with regional stakeholders from standardization, national agencies, accident insurance, and safety verification bodies.

In order to create a space for conducting these protocols, state-of-the-art testing facilities will be established at partner

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sites. These shared safety facilities will offer training, access to measurement systems for validation as well as support in using the toolkit and applying the protocols for interested third parties.

In addition to that, realistic trials will be carried out in the scope of financial support for third parties to stress test the toolkit and protocols with specific use-cases, and to provide background research and experimental data to determine best practices.

B. EUROBENCH

The European project EUROBENCH (*European robotic framework for bipedal locomotion benchmarking*; www.eurobench2020.eu) will use benchmarking as a method to assess the technology readiness level and to quantify how robotic solutions match user needs. System ability levels will be created to quantify performance of humanoid and wearable robots (prosthetics and exoskeletons) on comprehensive scales. This comprehensive benchmarking framework will be composed of two main outputs: a methodological framework which will include methods and metrics to calculate system ability levels and an experimental framework which will concentrate state-of-the-art test benches in two facilities to allow companies and researchers to perform standardized tests on advanced prototypes.

The methodological framework will be available as a software suite, including an interactive application to identify suitable testing methods, a scoring system, a data system for comparison with similar robotic systems and a decisional support system. The latter will help identify technical features that should be improved and predict future levels of system abilities that can be reached. The aim of this software is to facilitate the use of benchmarking methodology at all levels from research to pre-commercial prototyping. To ensure global consensus on this methodology, the project consortium will collaborate with other EU projects and organizations in Europe.

Similar to the realistic trials in the COVR project, EUROBENCH will offer financial support to third parties interested in designing and developing specific test benches or benchmarking methods or in using the framework to validate its outputs. The results will be used to mature the experimental benchmarking framework.

III. Discussion

While the two presented projects focus on different aspects (benchmarking and safety evaluation), they have a common goal: encouraging the development of new innovative technologies and enabling those to be ready for market. Both projects focus on the assessment of certain abilities or skills of robots interacting closely with humans and are making use of comparable methodologies. A software tool will identify relevant system abilities and safety skills and lead the robot developer to the applicable tests. Moreover, both projects aim to establish state of the art testing facilities and offer financial support for third parties that are interested in providing background research or evaluating the project services to provide input for achieving the project goals.

There are safety skills that can also be relevant system abilities / performance skills. Take, for example, the physical human robot interaction. Interaction forces are a very relevant aspect in safety of rehabilitation robotics which often are in continuous physical contact with the patient. This is especially challenging in neurological patients, where impaired sensation and physical changes like denervation constitute additional risk factors for too high pressure on patient's soft tissue [4].

Also in the field of performance of rehabilitation robots, physical human robot interaction is a key aspect discussed in many studies. While guidance of motion activities is one of the main functions of rehabilitation robots, it is widely discussed whether too much guidance can induce slacking and reduce the training effect [5]–[7]. Therefore, a certain amount of interaction force between robot and human might be of need to reach the optimal training effect. This has to be balanced carefully with safety considerations so that pressure sores and excessive joint forces are avoided.

However, the assessment of interaction forces between human and robot poses a major challenge. There is a lack of methods for continuously measuring detailed interaction force distributions in close interaction scenarios as present in exoskeletons or end-point manipulators with a shell for the arm or other limbs [3]. Especially with regard to shear forces, measuring methods as well as allowable limit values are still to be developed.

IV. Conclusion

Two European projects focusing on assessment of robotics have been presented. Human robot interaction force has been identified as one example for issues equally present in both benchmarking and safety evaluation of rehabilitation robotics.

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Pilot study: submaximal force control training for robotic therapy.

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***Abstract*— We investigate the use of submaximal force production as a targeted functionality in a rehabilitation task for early rehabilitation after stroke. We present the detailed assessment of related metrics of force production and position control, their correlation with submaximal force production control learning and their feasibility for robot–mediated therapy after stroke.**

I. INTRODUCTION

RECENT projects highlight how motor learning and a high level of attention control can potentially improve submaximal force production during recovery. Stroke patients might benefit as this pathology affects each year to 17 million people worldwide, being the second leading cause of disability [1]. We already provided preliminary evidence of the facilitation of learning processes from a kinematic point of view in healthy subjects with robotic devices [2]. Robotics can be used not only as standalone devices, but also in combination with virtual environments, providing the possibility of showing the patient and the physiotherapist the feedback of the performance of the task, which has been proven to improve rehabilitation [3]. In our previous work, we introduced the use of "tacit adaptability" (TAd) –a symbiotic control strategy based on biomimetic mechanisms, which is based on "tacit learning" [4]– with a stroke patient [5], walking on a treadmill, modulating the compliance with attention levels estimated from EEG signals. Marchal–Crespo et al. [6] 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.

This study focuses on the assessment of detailed metrics of force production and position control and their correlation with submaximal force production control learning, as improving regularity in submaximal force production might help improve functionality and reduce disability [7] during a new task consisting in maintaining the position for early rehabilitation after stroke. Our aim is to characterize the capacity to perform the precision task of maintaining the position with a submaximal force production in healthy subjects, by using the game we have designed that addresses the important factors for motor training: precision, speed, and path directness toward the specific targets presented on the screen [8]. We provide a novel approach in using TAd 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"[9] to try accelerate the rehabilitative process.

Transcranial Magnetic Stimulation (TMS) is the technique that allows the assessment of the corticospinal excitability in a non–invasive way [11]. The tibialis anterior (TA) dorsiflexor muscle is fundamental in the swing and heel strike phases of the gait [12]. 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 (motor evoked potentials) were found [13]. This technique has already been used in the literature to assess the TA excitability before and after lower limb trainings with motor imagery + robot–assisted dorsi–plantarflexion [14]. To check the suitability of the subjects for the experimental study, it is important to pass a screening questionnaire.

II. MATERIALS AND METHODS

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

A. Experimental Platform

A Motorized Ankle Foot Orthosis (MAFO) is used for this study, with a torque control. This robotic platform permits to exert controlled torque profiles to the ankle joint of the subject. The TAd module is explained in Fig. 1, as well as the rest of the platform.

B. Participant

One healthy subject, right–handed (Waterloo footedness [10]), 23 years old, was enrolled for this experiment.

C. Task

The experiment consisted in following the trajectories depicted via the visual paradigm, while the robot disturbed the movement by performing plantar and dorsiflex interleaved torque patterns (see Fig. 2 for explanation on the torque profiles). The aim was to learn how to compensate the perturbations to follow the trajectory in the screen, along three sessions, of 61 trajectories: 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.

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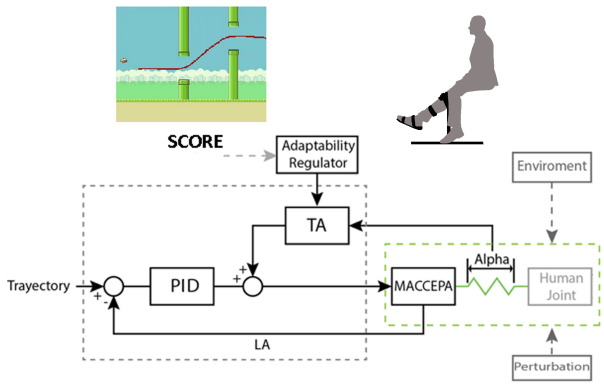

Fig. 1. Experiment set–up. The controller of the robotic platform consists on a zero torque controller (PID), with the addition of the TAd component (TAd constant $-K_{TA}-$ multiplied by alpha, angle between the robot and the subject, proportional to the interaction), modulating K_{TA} with the score. The user controls the position of the bird with the angular position of the ankle.

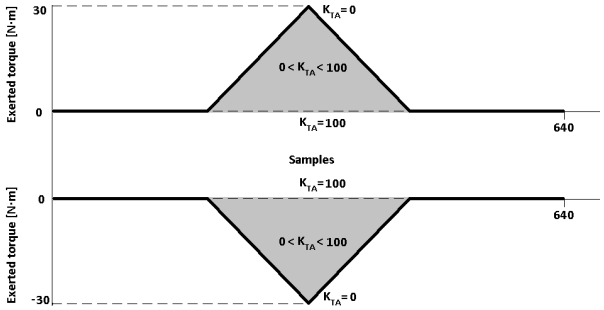

Fig. 2. Torque patterns. Torque to dorsiflexion (up) and plantarflexion (down) direction, with the behaviour of the TAd module: 1) $K_{TA} = 100$ leads to zero–torque control; 2) $K_{TA} = 0$ leads to regular torque control, so up to 16 N·m; and 3) K_{TA} between 0 and 100, closer to zero–torque control the higher K_{TA} is.

D. TMS assessment protocol

We performed TMS assessment before the first session, and after the last session (just after the last training, 30 minutes after, and 24 hours after). We used a cap where we marked inion, vertex, and the hotspot for the TA for repeatability on the measure.

III. Results

In the results we observed reduction trend on the RMSE, as well as a clear increment on the excitability on the TA (see Fig. 3).

IV. Conclusions and Future Work

The observed improvement in terms of reduction on error along the sessions suggests that the protocol may be a successful training for motor control. The increase on the excitability of the TA seen on the MEPs suggests potential plasticity, not only LTP(long term potentiation)–like, post 30 minutes; but also long lasting plastic effects (after 24 hours).

Our next work includes extending the protocol to a group of intact subjects to statistically prove the validity of the training, and its suitability for robot–mediated therapy after stroke.

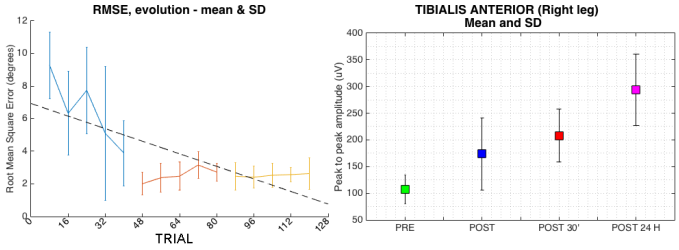

Fig. 3. Left) RMSE during each training session, in groups of 8 randomized trajectories. Dotted line represents the linear fitting of the data. Right) Tibialis Anterior MEPs after TMS for the four different assessments.

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The NISCI Project.
Antibodies against Nogo-A to enhance plasticity, regeneration and functional recovery after acute spinal cord injury, a multicenter European clinical proof of concept trial.

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***Abstract*---Until now there are no medical treatment options for para and tetraplegic patients after Spinal Cord Injuries (SCI). SCI affect the quality of life and the ability to work in the majority of patients in a severe and dramatic way. The social and economic burden of life-long care including frequent secondary complication is enormous. The NISCI project proposes to conduct a state placebo controlled multicentric clinical trial to assess the efficacy of anti-Nogo-A antibody therapy to significantly improve the neurological recovery and functional outcome of spinal cord injured patients.**

I. Introduction

The incidence of spinal cord injury is about newly injured 10'000 people per year in the EU, and due to an almost normal life expectancy more than 200'000 patients are living with a spinal cord injury in the EU. The impact on the individual quality of life is high, and social costs are enormous.

Recent preclinical research in animal models succeeded to greatly enhance axonal sprouting, fiber regeneration and neuroplasticity following injuries of brain and spinal cord. Regeneration of interrupted nerve fiber tracts and plastic "hardware" changes in the adult central nervous system (CNS) of mammals and humans are extremely restricted, a phenomenon which represents a main reason for the low degree of recovery following spinal cord injury (SCI) and brain injury (Schwab, 2014). Important molecular impediments that form the basis of this phenomenon are proteins expressed in CNS myelin, which inhibit neurite growth after CNS injury. One of the most potent neurite growth inhibitory molecules in myelin is Nogo-A, a membrane protein comprising multiple inhibitory domains that activate independent receptors (Schwab, 2010; Schwab and Strittmatter, 2014).

Monoclonal antibodies against Nogo-A have been shown to neutralize the inhibitory activity of purified or recombinant Nogo-A, oligodendrocytes and CNS myelin in vitro (Caroni and Schwab, 1988; Chen et al., 2000). More importantly, a number of publications over more than 15 years have shown that function blocking anti-Nogo-A antibodies mediate significant improvements in functional recovery in rodent models of SCI (Freund et al., 2009; Schwab and Strittmatter, 2014), non-traumatic brain injury (Wahl et al., 2014) and traumatic brain injury. Anti-Nogo-A antibody treatment facilitates neuroregeneration at the anatomical level in rodents and two non-human primate models of SCI. Very similar results on the anatomical and functional level were obtained in Nogo-A knock-out mice, in rodents treated with Nogo receptor-derived function blocking fusion proteins or antibodies against the Nogo receptor associated protein Lingo-1 (Schwab, 2010; Schwab and Strittmatter, 2014).

These results warrant translation now to patients suffering from acute spinal cord injury.

The NISCI project proposes to conduct a state of the art placebo controlled multicentric phase II clinical trial in a consortium of seven leading European spinal cord injury centers to assess the efficacy of anti-Nogo-A antibody therapy to significantly improve the neurological recovery and functional outcome of spinal cord injured patients. The network involve: Spinal Cord Injury Center, Balgrist University Hospital (Coordinator), Zürich (Switzerland); Universitaetsklinicum Heidelberg (Germany); University College London (UK); Fundacio privada Institut de Riabilitacio Guttman (Spain); Fakultni Nemocnice VMotole (Czech Republic); Berufsgenossenschaftliche Unfallklinik Murnau (Germany); IRCCS Fondazione Santa Lucia (Italy); Klinikum Bayreuth GmbH (Germany); Ruhr-Universitat Bochum (Germany); ECRIN European Clinical Research Infrastructure Network (France); TP21 GMBH (Germany).

II. The NISCI Project: main purpose

The purpose of the NISCI study is:

1) to confirm in a network of seven leading European Spinal Cord Injury Centers the feasibility of administration, safety, and tolerability of the anti-Nogo-A antibody ATI355 in patients with acute cervical SCI;

2) to assess the efficacy of ATI355 to significantly improve the neurological and functional outcome of SCI patients;

3) to assess cutting edge number of biochemical and imaging biomarkers for their value of distinguishing groups of SCI patients with differing lesion severity and functional impairment as well as the ATI355 treatment effects.

III. Clinical Study: Phase I

A previous phase I clinical study using intrathecal

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application of a nerve fiber growth promoting antibody against the growth inhibitory protein Nogo-A has shown in patients with complete spinal cord injury that this treatment is safe and well tolerated. The present study will enroll patients with various degrees of complete to incomplete acute spinal cord injury for a double-blind, placebo-controlled trial to test the efficacy of this antibody therapy to improve motor outcome and quality of life of tetraplegic patients. The enrollment of patients with different degrees of spinal cord injury is considered essential to reveal drug activity and eventual proof of concept in a broad patient population.

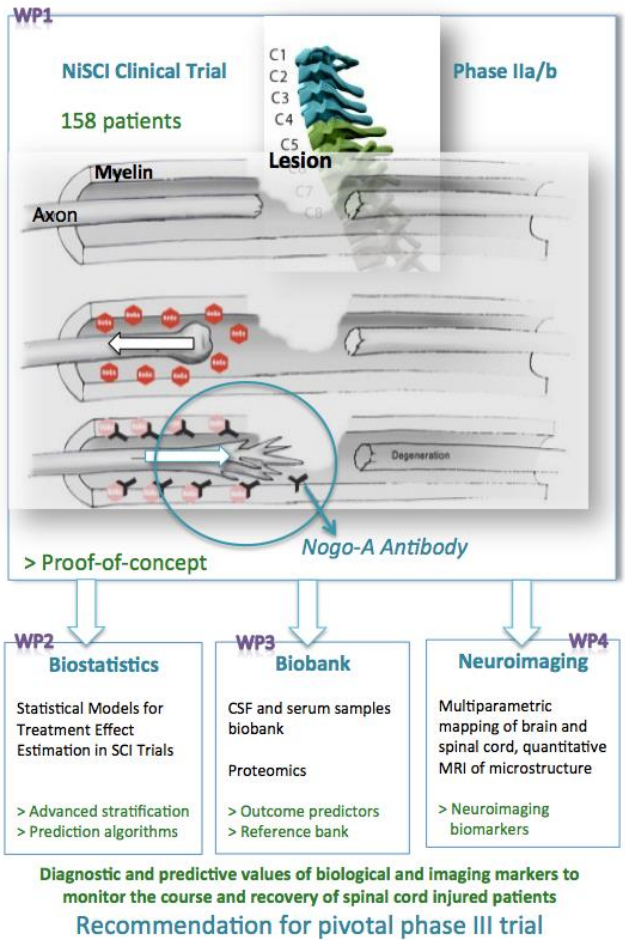

Figure 1: NISCI overall concept combines a clinical Phase II trial, biostatistics for effect estimation, novel quantitative magnetic resonance imaging (MRI) methods and the establishment of a biobank based on serum and cerebrospinal fluid samples.

Advancements in clinical trial design, improved prediction algorithms of clinical outcomes and development of surrogate markers (in cerebrospinal fluid/serum and by neuroimaging) will allow for scrutinizing the effectiveness of this novel treatment in an unprecedented way. A positive outcome of this trial will represent a breakthrough for the future therapy of spinal cord injuries and beyond (traumatic brain injury, stroke, multiple sclerosis).

ACKNOWLEDGMENT

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EEG-based Assessment and Adaptation of Novel (Robotic) Neuro-rehabilitation Therapies

Joaquín Peñalver-Andrés, Karin A. Buetler, and Laura Marchal-Crespo

Abstract— **Understanding the underlying mechanisms of motor learning is a crucial aspect in neuro-rehabilitation. Skilled movements are a result of several sequential cognitive and motor achievements: from task understanding to correct muscle recruitment and activation. We believe that, by following subjects cognitive and neuro-motor performance at each time point during motor training, an optimal learning process is possible. The methods and research plan to achieve such a goal are presented in this paper. We hope that the results of this study or project will help us providing clinicians with means to optimize neuro-rehabilitation.**

I. INTRODUCTION

Authors in the field of neuro- rehabilitation agree that motor recovery (i.e. motor neuro- rehabilitation) is a form of motor learning[1]. Motor learning is a complex neurocognitive and motor process and several authors have made attempts to define its phases. Fitts[2] proposed that motor learning follows three phases. At an early stage of learning, subjects find themselves on a more cognitive phase, where trial and error is a tool to discover the underlying rules to perform in the learning environment. Following, an associative phase, where subjects start building up strategies by linking stimuli from the learning environment to meaningful entities. Finally, subjects reach a stage of expertise, i.e. autonomous phase, where motor strategies are consolidated in memory and fine-tuned to achieve levels of skillful performance. According to this model, motor learning may be optimized by adapting motor training to each phase of learning, i.e. the individual skill level of the practitioner.

A well-known motor learning paradigm, the so called Ecological Dynamics of Motor Learning[3], suggest the representative learning design framework to train complex tasks (e.g. daily life activities). According to this framework, two main requisites have to be followed: the task should dynamically evolve in time in terms of difficulty (providing users with the chance to cherry pick sensory information from the environment) and task progression to the next challenge level should be scheduled in a self-paced way (so that success is always granted).

These theoretical precepts find empirical proof in the motor learning literature. For example, haptic and visual guidance and feedback have different effects on different populations (e.g. beginner and experts). Namely, robotic haptic guidance was found to be particularly helpful for initially less skilled subjects[4]. Also, it has been shown that robotic assistance has varying effects on training different aspects of a movement (e.g. timely or spatial features; see [5][6] for reviews). Further, it has been shown that the knowledge of specific task rules and task working principles (i.e. task understanding) correlates with task performance (e.g. in golf[7] or tennis[8] games). In line with these behavioral results, researchers have found progressive changes in cortical brain structures when subjects are provided with hierarchical information about the underlying working principles of a system[9]. These finding underline the importance of the feedback provided during training for therapy outcome.

Together, theoretical models and empirical evidence on motor learning suggest that motor learning is hierarchically modulated by neurocognitive and motor processes, namely task understanding and the recruitment of motor strategies. Yet, less is known about how to adapt motor training paradigms to support the hierarchical processing to optimize motor learning[10].

Within this project, we aim to identify the neurocognitive markers for task understanding and recruited motor strategies during motor learning via Electroencephalography (EEG). The gained information will then be used to test an automatized training paradigm which modulates the training environment to support task understanding and recruitment of motor strategies in real time. We hope to promote, in this way, optimal motor learning during motor neuro-rehabilitation.

II. HYPOTHESIS

EEG event-related potential (ERP) components, concretely the P300[11] and the error-related negativity (ERN)[12], have been shown to capture attentional engagement of cognitive processes, thus, this kind of signals features may be used to evaluate the level of task understanding in a given subject.

Further, we hypothesize that an anterior-posterior shift of brain activity from perceptual to motor areas (passing from frontal abstract reasoning and central associative areas)[7] might occur during motor learning. This shift might be captured by analyzing quasi-stable EEG network configurations (μStates) and by performing source localization [9].

Finally, EEG μStates have shown to reflect the spatio-temporal composition of neuro-motor cortical states. In [13], it has been shown that subject-specific μStates spatio-temporal composition correlates with specific voluntary motor patterns. Therefore, we hypothesize that correct versus incorrect recall of motor strategies will be reflected in

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a modification of the spatio-temporal composition of the μStates.

III. METHODS

To characterize and assess task understanding and recall of correct motor strategies, a series of experiments will be conducted. A final experiment will address the effect of modulating, in real-time, the training environment to support task understanding and recruitment of motor strategies on motor learning. A total of three experiments will be conducted, primarily with healthy subjects (with a minimum sample of 30 subjects per experiment). Clinical transfer will be evaluated in patients in collaboration with the Inselspital (Bern, Switzerland).

A. Experimental Setup

The system to be used comprises of three main elements(see Fig.1): the EEG system Ⓐ, the virtual environment Ⓑ and the Intelligent Control Unit Ⓒ. A three degree-of-freedom robot will be used to provide haptic feedback and a virtual reality system will be used to provide visual input to the subjects. A 128 electrodes geodesic EEG system, will be used to register the neuro-physiological signals during motor task performance.

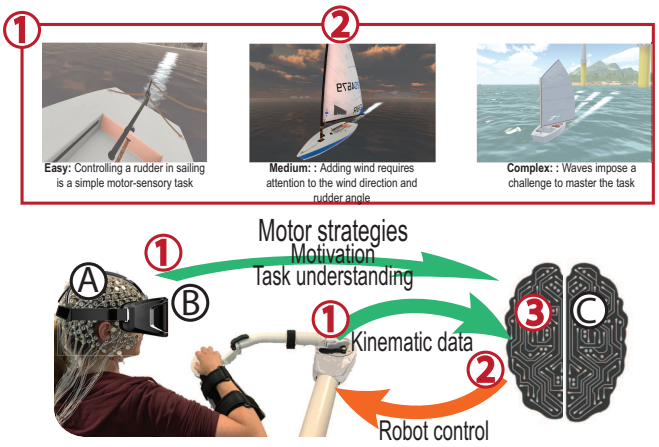

Fig. 1. Project layout diagram: Green and red arrows are inputs and outputs from the intelligent system. Letters refer to the different sub-systems used. Numbers relate to the elements progressively included at each experiment.

B. Task & Experiments

Experiment ①: *Observing the effects of task difficulty on cognitive and motor neural correlates* . This experiment is aimed at characterizing and assess the impact of task difficulty on electrophysiological and behavioral correlates of task understanding and motor strategy recruitment. The robot is kept in compliant mode (i.e. free movements) and the subject is asked to perform a task in three levels of difficulty. Motion data of the robot and EEG signals are recorded and off-line processing.

Experiment ②: *Observing the effects of robotic training strategies on cognitive and motor neural correlates*. The aim of this experiment is to understand the effects of using robotic supportive versus resistive strategies on neurocognitive and motor performance. In this experiment, a the level of task difficulty is fixed. Motion data of the robot and EEG signals are recorded and off-line processing is performed.

Experiment ③: *Controlling the neurocognitive and motor neural correlates of motor learning*. The goal of this final experiment is evaluating the effects of automatically adapting task parameters (see experiment 1) and robotic training strategies (see experiment 2) to promote optimal task understanding and recall of correct motor strategies on motor learning.

IV. CONCLUSIONS

With this project we hope to advance the boundaries of knowledge in the field of motor learning, namely to provide insights into the underlying mechanisms of human motor learning, which may be useful for designing more effective training protocols for the treatment of motor disorders.

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Synergy-based Classification to Anticipate Reaching Direction Identification in Stroke subject for Robotic Arm Teleoperation

Stefano Tortora, Stefano Michieletto, and Emanuele Menegatti

***Abstract*— A high level of disability and muscle weakness can prevent an effective identification of user intention, introducing high time delays in controlling robotic devices. In this paper, a muscle synergies extraction algorithm is coupled to a Gaussian Mixture Model (GMM), in an evidence-accumulation framework, to anticipate the detection of reaching direction from surface electromyography (sEMG). The proposed method has been tested with online hardware-in-loop simulations to control a UR10 manipulator robot. On average, the system identifies the desired direction after $32.8 \pm 6.2ms$, with an accuracy of $96.8 \pm 2.1\%$ for a healthy subject, and after $47.6 \pm 13.4ms$ for a stroke patient, with an accuracy of $81.4 \pm 12.8\%$. We believe that the proposed method can improve the robustness of myoelectric controlled devices for stroke motor rehabilitation and assistance.**

I. INTRODUCTION

Continuous and direct myoelectric control of robotic devices could be unfeasible for severely affected stroke survivors, due to muscle weakness and failure of central motor drive [1]. A discrete control approach generally increases the reliability of the system. However, it introduces higher time delays between the detection of user motion intention and the corresponding command to the robotic device.

This paper extends a novel synergy-based classification method developed by our research group [2], that is able to recognize reaching direction with high accuracy in the early phase of motion. Once the high-level motor command is detected, a robotic manipulator guides the movement towards the desired target in a shared-control approach. The performance of the proposed method has been tested on both a healthy and a stroke subjects, with online hardware-in-loop simulations.

II. MATERIAL AND METHODS

A. Experimental data

Kinematic data and sEMG data from 16 upper limb muscles have been experimentally recorded at the IRCCS Fondazione Ospedale San Camillo, Venice, Italy. They refer to a right-handed female healthy subject (H1, age, 32 years) and to the right paretic limb of a male patient (S1, age, 60 years) with left nucleo-capsular stroke. The protocol is shown in Fig. 1. EMG data have been concatenated and visually inspected for channels corruption.

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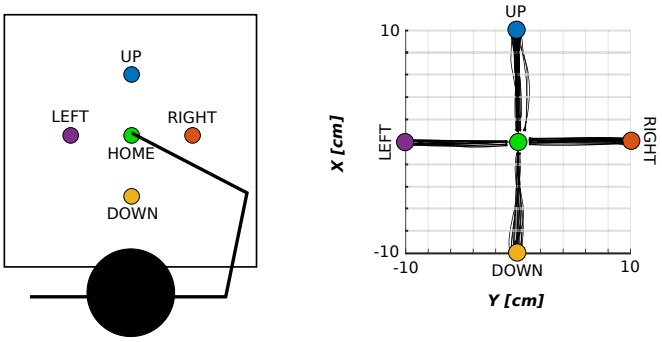

Fig. 1. Experimental protocol for data collection (left). At each trial, the subject has been asked to reach one among four target positions at 10 cm from a 'HOME' position. The recorded trajectories for the healthy subject on the coronal plane are also shown (right).

B. Offline model training

The control architecture to train the classifier and control the robot is shown in Fig. 2.

To reduce the variability in stroke subject dataset, compared to the more repeatable patterns of the healthy subject, the trials have been sorted according to two kinematic assessment metrics, the *aiming angle* and the *length path ratio* [3]. The 10% of trials that diverge the most from a straight line have been removed from the dataset.

Raw signals from each channel have been preprocessed to extract the muscle activity envelopes [2]. The EMG envelopes have been factorized by applying the Non-negative Matrix Factorization (NMF) algorithm. NMF extracts the subject-specific muscle synergy matrix H, containing N_{syn} time-invariant and task-independent synergy modules, and the N_{syn} - dimensional matrix W of activation coefficients over time. The $N_{syn} < M$ has been found to have a robust agreement between the original and the reconstructed dataset, by looking to the Variance-Accounted-For (VAF) [4]. A Gaussian Mixture Model (GMM) has been trained for each subject to model the N_{syn} synergy activation vectors $w(t)$ at each time stamp, alongside with the class ζ corresponding to the target the user is going to reach in the considered trial.

C. Online robot control

The activation coefficients vector $w(t)$ on the testdataset has been computed by solving a least squares problem with non-negative constraint, from the muscle synergy matrix H computed in the training phase. For each observation w, the probability to select a specific target $\hat{\zeta}$ is computed by means

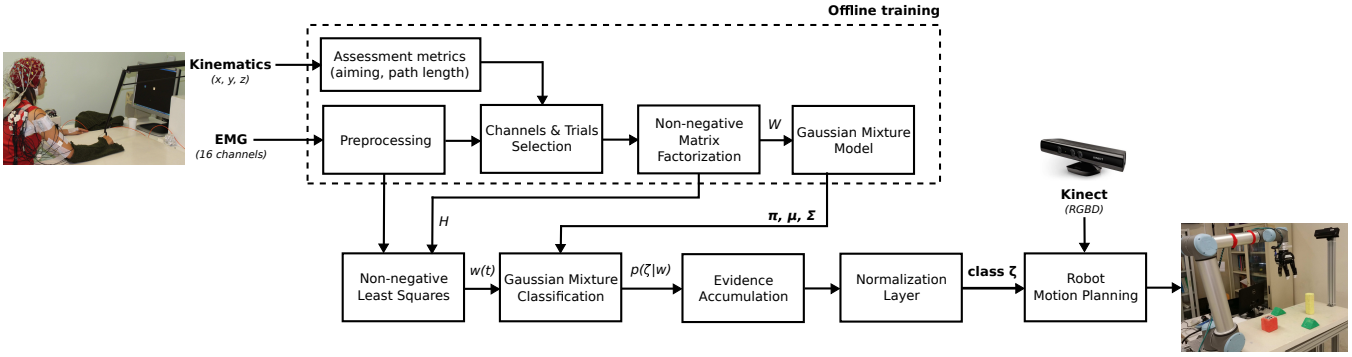

Fig. 2. Online control architecture. The blocks inside the dotted rectangle have been computed offline to extract the muscle synergy matrix and to train the classifier. The motion planning towards the desired object is computed for the manipulator, based on the visual feedback from a Microsoft Kinect camera.

of the conditioned probability density function:

$$p\left(\hat{\zeta}|w\right) = \sum_{k=1}^{K} \frac{\pi_k \mathcal{N}\left(w\,|\mu_{w,k}, \Sigma_{w,k}\right)}{\sum_{i=1}^{K} \mathcal{N}\left(w\,|\mu_{w,k}, \Sigma_{w,k}\right)} E\left[\zeta_k\,|w\right] \quad (1)$$

Finally, we estimated the class related to w by selecting the maximum of the accumulated probability per class along time. The performance of the method has been tested for each subject by means of 5-fold cross-validation procedure. For robot control, a command is identified and sent if the evidence has been accumulated for at least 20 ms and the difference between the two classes with the highest probability is > 0.5. Once the command is sent, the position and the orientation of the desired target object on the working bench is identified through a Microsoft Kinect camera and the trajectory of the UR10 manipulator robot is generated by the *MoveIt!*[1] motion planning framework within ROS.

III. RESULTS

From the synergies extraction procedure, the cross-validation has identified $N_{syn} = 4$ for the healthy subject and $N_{syn} = 3$ for the stroke patient. The average classification performance and the performance for each target are shown in Fig. 3A and Fig. 3B, for the healthy and the stroke subjects, respectively. For healthy subject, the criteria to send a command are met after $32.8 \pm 6.2ms$ on average, with an accuracy of $96.8 \pm 2.1\%$. The stroke patient presents a slightly worse behavior, with the command sent after $47.6 \pm 13.4ms$ on average, with an accuracy of $81.4 \pm 12.8\%$.

IV. DISCUSSION

As expected from literature [4], a reduced number of synergy modules has been extracted for the stroke subject, due to a reduction of motor control and coordination. Results show that classification accuracy saturates for both healthy and stroke subject around 10% of reaching distance (about $20ms$). During online simulation, the system has been able to recognize and send the correct commands with a time delay that is lower than the electro-mechanical delay (EMD), about $80ms$ for upper limb movements.

[1]https://moveit.ros.org/

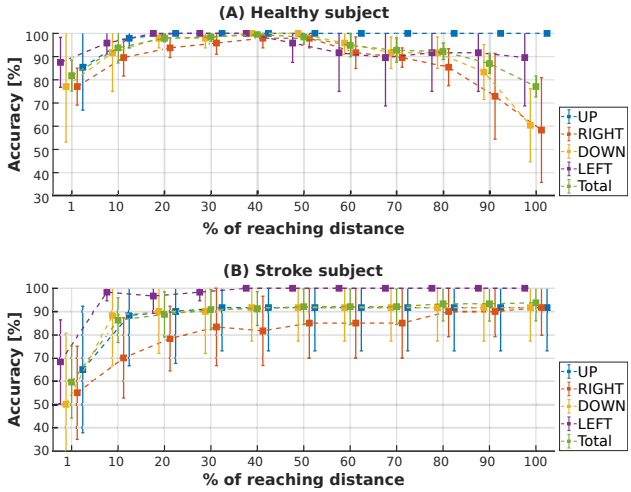

Fig. 3. Classification accuracy over the reaching distance, computed for each target and the accuracy on the total test dataset (in green) for the healthy (A) and stroke (B) subjects.

V. CONCLUSION

Given the promising results of this work, we aim to implement subject-specific criteria for commands sending and to test the system on a bigger population. We believe that assistive technology could benefit from an accurate and fast algorithm for motion classification, particularly when a reduced muscular activity affects the identification of user intentions.

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Down-Conditioning of Soleus Reflex Activity using Mechanical Stimuli and EMG Biofeedback

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***Abstract*— Spasticity is a common syndrome caused by various brain and neural injuries, which can severely impair walking ability and functional independence. To improve functional independence, conditioning protocols are available aimed at reducing spasticity by facilitating spinal neuroplasticity. This down-conditioning can be performed using different types of stimuli, electrical or mechanical, and reflex activity measures, EMG or impedance, used as biofeedback variable. Still, current results on effectiveness of these conditioning protocols are incomplete, making comparisons difficult. We aimed to show the within-session task-dependent and across-session long-term adaptation of a conditioning protocol based on mechanical stimuli and EMG biofeedback. However, in contrast to literature, preliminary results show that subjects were unable to successfully obtain task-dependent modulation of their soleus short-latency stretch reflex magnitude.**

I. Introduction

Spasticity is a common syndrome caused by various brain and neural injuries. Spasticity, clinically defined as a velocity-dependent resistance of a muscle to stretch [1], can severely impair walking ability and functional independence. It is mainly caused by an exaggerated muscle stretch reflex, i.e. muscle hyperreflexia [2]. To improve the functional independence, two types of conditioning protocols are available aimed at reducing hyperreflexia by facilitating spinal neuroplasticity. First, at muscle level EMG biofeedback of either H-reflexes elicited with electrical stimuli [3] or short-latency stretch reflexes (SSR) elicited with mechanical stimuli can be used [4]. Second, at joint level biofeedback of reflexive joint impedance together with mechanical stimuli can be used [5].

The impedance-based protocol has multiple advantages compared with the EMG-based paradigms. First, the modulation is targeted at joint level, which could help to better facilitate functional improvements [6]. Second, significant task-dependent training effects were already attained after 2, instead of 4-6, sessions. Third, compared with the H-reflex paradigm, mechanical instead of electrical stimuli are used. This could improve participant comfort and general applicability to joints across the body. Unfortunately, the long-term effect as well as the clinical implementation of the impedance-based protocol have not been investigated yet.

To evaluate the effectiveness of these conditioning protocols, it is essential to have an insight in the percentage reduction of both task-dependent and long-term reflexive activity per training session for each protocol. Currently, complete results are only available for the H-reflex protocol, thus it is unknown which of the three protocols would be best to eventually use in the clinic. Moreover, the combined results of all protocols will also give insight into the role of the type of stimulation, electrical versus mechanical, and the type of biofeedback, EMG versus impedance, during conditioning. This paper shows preliminary results for the task-dependent adaptation of a protocol based on EMG feedback of the soleus SSR elicited with mechanical stimuli.

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II. Material and Methods

Nine healthy adults (3 female, 22.9±2.4y) participated in this study. The study was approved by the EEMCS Ethics Committee of the University of Twente and all subjects gave written informed consent. The experiment was designed in similar fashion to [3].

The protocol consisted of 5 baseline sessions followed by 18 conditioning sessions with subjects participating in 3 sessions per week. In every session, subjects were seated with their right foot attached to an actuator (Moog, Nieuw-Vennep, the Netherlands) using a rigid footplate and Velcro straps. The system applied one degree of freedom perturbations in the sagittal plane around the ankle joint to elicit the stretch reflexes. The perturbation profile had the following characteristics: an amplitude of 8.1°, a maximum velocity of $190^\circ/s$ and a maximum acceleration of $7000^\circ/s^2$.

In a baseline session, 225 control reflexes were elicited. For these control reflexes, subjects were asked to maintain a stable level of background activity set as percentage of soleus maximum voluntary contraction (MVC), measured at the start of the session. The desired level of background activity was reached by pressing on the footplate, which was kept in position by the actuator. In a conditioning session, first 25 control reflexes were elicited followed by 225 conditioned reflexes. For the conditioned reflexes, subjects were asked to decrease the SSR magnitude, while keeping a stable background activity level. Visual feedback was provided for both background activity and SSR magnitude. Reflexes were only elicited, if subjects maintained a stable background activity for a period between $2.25s$ and $4s$, picked randomly to keep perturbations unpredictable. Moreover, subjects were urged to relax the first $4s$ after every reflex to avoid fatigue.

Muscle activity of the soleus was measured at 2048 Hz using a Porti (TMSi, Oldenzaal, the Netherlands). For data analysis, the EMG signals were high-pass filtered (2nd-order Butterworth, 10 Hz), rectified and normalized with MVC.

Background activity was calculated using a 100ms window before perturbation onset. SSR magnitude was calculated as the area under the curve in the reflex interval, a 20ms window with a subject specific start after perturbation onset (typically 43ms), minus the background activity.

III. Results

The preliminary results of the executed experiment focus on the within-session, task-dependent adaptation of the SSR magnitude using the differences between the conditioned and control reflexes. Based on the results of H-reflex experiments [7], task-dependent adaptation should be visible after 4-6 conditioning sessions. The baseline sessions, which were executed without subject instruction to reduce SSR magnitude, are used as reference as no within-session adaptation should occur.

Unfortunately, on average subjects show no task-dependent adaptation of the SSR magnitude during the conditioning sessions, see Fig. 1. To confirm, the task-dependent adaptation of the 5 baseline sessions and the last 5 conditioning sessions also show no statistical difference ($p = 0.45$, unpaired t-test). Individually, only 1 subject shows a significant effect between these groups of sessions ($p < 0.05$, unpaired t-test) with an average task-dependent reference of +8.6% during baseline and change of -3.3% during the last 5 sessions of conditioning. However, this is still about 5 times smaller than the -15% of task-dependent conditioning

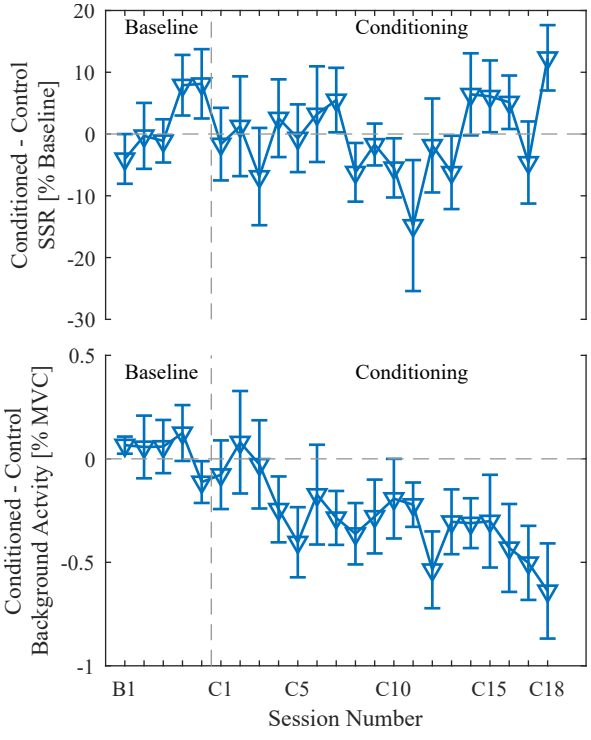

Fig. 1. *(Top)* Group average (± SE) conditioned SSR size minus control SSR size, i.e. task-dependent adaptation *(Bottom)* Group average (± SE) change in background activity conditioned minus control block accompanying task-dependent adaptation of reflexes

obtained with the H-Reflex protocol [7]. The group change in background activity accompanying the task-dependent reflex adaptation was significantly different between start and end of the experiment ($p < 0.05$, unpaired t-test), see Fig. 1. On average, background activity slightly increased during baseline sessions, 0.04% MVC, while it slightly decreased during the last 5 conditioning sessions, -0.44% MVC.

IV. Discussion and Conclusions

The goal of our experiment was to show the effectiveness of a SSR conditioning protocol based on EMG feedback and mechanical stimuli. In contrast to our expectations, subjects were unable to show within-session, task-dependent down-conditioning of the SSR magnitude. These results are not in line with literature, as previous research with the combination of mechanical stimuli and EMG feedback was successful in showing an overall conditioning effect [4] and long-term effect specifically [8].

Two aspects of the experiment could potentially cause a difference between our study and literature. First, on average a slight within-session decrease in background activity was observed during conditioning. However, a decreased background activity should help obtain a task-dependent reduction in SSR magnitude as motoneuron excitability is reduced. Second, task instructions were slightly different compared to the experiment of [4]. In our study, subjects were instructed to press on the footplate, which was kept in position by the actuator. Contrarily, in [4] subjects were requested to hold a steady position while an actuator delivered a constant bias torque to their joint. The potential effect of the difference in task instruction on task-dependent adaptation will be subject for further research. Moreover, once task-dependent adaptation is achieved, also the across-session long-term effects can be evaluated.

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Investigating Concurrent Neuroplasticity and Changes in Level of Functionality in SCI Individuals

Kasper K. Leerskov, Lotte N. S. Andreasen Struijk and Erika G. Spaich

Abstract — **This paper describes a roadmap for investigating concurrent plastic changes and functional development in spinal cord injury individuals following therapy. Relevant plastic measurements and the expected analysis of these measurements are presented.**

I. Introduction

FOLLOWING a spinal cord injury, the central nervous system (CNS) of SCI individuals undergoes a variety of adaptive plastic changes, consisting of anatomical, physiological, and functional changes [1] in the sensory-motor cortex, the brainstem and the spinal cord above and below the injury [2]. Reverting these adaptive changes is associated with better outcomes for the SCI individuals [1], [3].

Restoration of locomotion in SCI individuals is of high priority and is believed to reduce a variety of side effects from being immobile [4], if achieved. Rehabilitation of locomotion using robotic gait training aims at exploiting plasticity [3] and has been shown to induce plastic changes resulting in e.g. increased inhibition of the soleus H-reflex [1], increased activation of motor cortex [5] and increased cortical modulation of spinal circuits [6].

Evidently, the changes following SCI are present at multiple levels of the neuroaxis, affecting in various ways the functionality of the nervous system [1], [2]. For a more extensive review of the plastic changes associated with SCI, see [1], [3], [7]. The complexity and extensiveness of plasticity following SCI makes it inherently difficult to investigate [2].

As the improvements that may be seen following gait training in SCI individuals, are expected to be the result of concurrent plastic changes at multiple levels along the neuroaxis [1], [3], it has been proposed to investigate these plastic changes at three levels in parallel: The descending pathways from the motor cortex to the lower limbs, the ascending pathways from the lower limbs to the sensory cortex, and the intrinsic inhibitory circuits of the spinal cord and relate these to a measure of the SCI individuals' capability [8].

The present paper suggests a framework for evaluating plastic changes at these levels.

II. Methods

A. Study design

To appropriately investigate plastic changes, it is critical to continuously monitor plastic changes in SCI individuals throughout their therapy. Therefore, several measurements should be taken, with appropriate periods of time between measurements e.g. 2-3 months. For comparison, obtaining reference measurements from healthy subjects, could be considered, as changes could then be assessed as proportional change from initial values towards "normal" values.

B. Descending pathways

Investigations of the descending pathways have the purpose of assessing the subjects' capability to voluntarily activate cortical areas. This is important as supraspinal control is involved in initiating movement and navigating complex environments [9]. The investigation is proposed to be done during attempted movement, while monitoring changes of the motor-related cortical potential [10] using EEG and changes in resulting muscle activity using EMG. It is proposed to monitor muscle activity in both a proximal and a distal leg muscle, as both are needed to achieve gait, yet the strongest rehabilitation is expected in the proximal muscles [11].

C. Ascending pathways

The assessment of plastic changes in the ascending pathways, has the purpose of investigating the change of sensory pathways related to gait. The sensory feedback achieved through movements of the leg is very complex, which is why investigations using somato-sensory evoked potentials, using electrical stimulus to the tibial nerve, seems appropriate, as it assesses both the tactile and proprioceptive pathways [12]. Changes in the observable potentials in the EEG should be assessed.

D. Intrinsic inhibitory spinal circuits

Different spinal circuits could be investigated and in a variety of ways; however, the conditioned soleus H-reflex has been widely used in research of changes in several intrinsic networks following locomotor training and is related to gait deficits in SCI individuals [1] and is therefore proposed. Additionally, different spinal circuits can be assessed simply

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by changing the timing between the conditioning and the testing pulse [1] e.g. reciprocal, presynaptic and homosynaptic inhibitory circuits. Furthermore, the stimulus location could be the same as used to elicit somato-sensory evoked potentials. Changes in the inhibition/facilitation of the soleus H-reflex should be assessed.

E. Functional measurements

When considering functional assessments, it is important to use a measurement relevant to the subjects' functional capabilities. SCIM III is a reliable and valid measure of the assistance needed for SCI individuals to complete a variety of everyday tasks [13] and therefore seems appropriate.

F. Statistics

The plastic changes observed should all be assessed for significant changes overtime. Additionally, the plastic changes following therapy get even more relevant, if correlation to functional improvements can be found. Therefore, it is suggested to investigate correlations between SCIM III scores and all the obtained measurements for plastic changes.

III. Results

A. Descending pathways

The results following investigations of the descending pathways, could describe the changes in the motor-related cortical potential based on peak-negativity amplitude and latency, as well as peak-to-peak amplitude. Additionally, changes in muscle activity could be assessed as max and mean amplitude during the contraction, as well as the proportion of samples were the muscle activity is significantly different from rest.

B. Ascending pathways

The results of investigations of the ascending pathways, could describe changes in observable components, as well as changes in the components' amplitude and latency.

C. Intrinsic inhibitory spinal circuits

The investigations of the intrinsic spinal networks should describe the change in inhibition/facilitation of the different networks assessed.

D. Functional measurements

The investigations of functional capability should describe the total change in score of SCIM III as well as the changes in the subcategories of SCIM III.

E. Statistics

The statistical investigations should describe any significant changes in the plastic measurements, as well as the correlation between each measurement and SCIM III.

IV. Discussion

In the present paper, a roadmap for assessing concurrent plastic changes following gait training of SCI individuals in ascending and descending neural pathways, and intrinsic spinal networks has been presented. The roadmap has been developed to emphasize the complexity of plastic changes and the need for evaluating concurrent plastic changes simultaneously, to a higher degree than current efforts. The suggested measurements have been chosen out of consideration for simplicity of an experimental setup and the realizability of an extensive plasticity investigation.

V. Conclusion

The presented roadmap is to be used in future studies, examining the concurrent plastic changes in SCI individuals receiving therapy, and the respective correlation between plastic changes and the functional capability of SCI individuals.

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Decoding intracortical activity to predict rat locomotion

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***Abstract* — This contribution to Summer School on Neurorehabilitation 2018 (SSNR2018) describes our progress in developing a rat model for a functional electrical stimulation (FES) neuroprosthesis for rehabilitation following spinal cord injury (SCI). We first evaluated the quality of electromyography (EMG) and kinematics decoding results using neural data from an intracortical array implanted in the sensorimotor cortex. Spiking activity predicted EMG and kinematics with reasonable results. Our future goal is to drive a brain machine interface (BMI) to restore locomotion after SCI using FES and evaluate its potential as a rehabilitative technology to improve general motor function.**

I. Introduction

RECOVERY of functional gait patterns after SCI requires modulation of motor cortex commands. FES is a promising approach that offers a mean to restore voluntary limb movements after spinal cord injury, when used in a BMI [1]. This involves recording cortical activity to decode an intended movement and then stimulating paralyzed muscles to execute the intended movement. We previously showed the potential of a FES-BMI to restore motor function after temporary paralysis in monkeys [2]. However, for ethical reasons, we need to identify another model that allows us to replicate paralysis symptoms and neural changes after SCI. We have identified an alternative in the rat model, in which the use of SCI is common.

There is also some evidence that peripheral stimulation, when synchronized with patients' voluntary effort, can further promote recovery by strengthening residual descending connections through activity dependent plasticity [3]. In that sense, our rat model can also be used to evaluate the potential of a FES-BMI for restoring and rehabilitating locomotion function following SCI.

This contribution presents the quality of electromyography (EMG) and kinematics decoding results using neural data from an intracortical array implanted in the sensorimotor cortex.

II. Material and Methods

Adult female adults were trained to run for ten consecutive minutes during different trials, with a steady stable pattern of locomotion in the same general region of the treadmill, at speeds ranging from 10-13 m/min. After completion of training, rats were implanted with intracortical arrays spanning the right hindlimb sensorimotor cortex and bipolar EMG electrodes in 6 muscles from the left hindlimb.

Following recovery, EMG, kinematics and neural data were simultaneously recorded whilst the rats walked on the treadmill. Hindlimb kinematics were recorded by tracking the 3D position of markers placed on bony landmarks. Cortical signals were obtained from spiking activity recorded in the intracortical electrodes. Multiunit spike rates were calculated in 50ms bins. EMG activity was high pass filtered, rectified, and integrated in 50ms bins. Sagittal plane joint angles were calculated for the hip, knee, and ankle from the recorded markers position every 50ms. We also calculated the limb vector angle as the angle between the markers at the top of the pelvis, the hip, and the toe.

Linear and non-linear filters were used to decode EMG activity and hindlimb kinematics from spike rates [2] [4]. Linear decoders were found by identifying optimal impulse responses between cortical activity and motor outputs, as described previously [2]. Non-linear decoders were recurrent neural networks (RRNs) [5]. Both types of decoders used a history length of 500ms of cortical activity. Decoders performance was evaluated by calculating the variability accounted for (VAF) with 10-fold cross validation.

III. Results

Predictions of kinematics using spike activity from intracortical array were good, with VAFs of 0.6-0.7. Predictions using non-linear filters (RNNs) were slightly better than those from linear decoders, but the improvement was minimal (~0.05-0.1). Predictions of individual EMGs (0.2-0.6) were poorer than predictions of kinematics.

IV. Conclusions and Ongoing Research

As a first step in the development of a rat model for a functional electrical stimulation (FES) neuroprosthesis for rehabilitation following spinal cord injury (SCI), we were

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able to obtain good predictions of kinematics and EMGs during rat locomotion, when decoding data recorded from an intracortical array. We believe that the accuracy of our decoders is sufficient to drive a FES-BMI.

Our future goal is to test cortically-controlled FES to restore locomotion after SCI in a rat model and evaluate its potential as a rehabilitative technology to improve general motor function. We expect that FES may strengthen residual descending connections. With repeated training, these strengthened connections might provide a substrate for functional voluntary movements. The experiments herein described are essential before translation to humans.

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Paired associative stimulation protocols with transcranial magnetic stimulation for motor cortex potentiation

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Abstract—**Paired Associative Stimulation (PAS) refers to a paradigm in which Transcranial Magnetic Stimulation (TMS) functions as an excitability potentiation tool over corticospinal motor pathway. By synchronizing this non-invasive cortical stimulation with a motor cortex activation stimulus, changes in synaptic strength and function are achieved. In this review, we detail a brief variety of PAS intervention protocols and their consequences.**

I. Introduction

NEUROPLASTICITY is the capacity of the brain cells to modify their structures as an adaptation to outcome changes. It is the biological mechanism of the learning and memory process that allows a potentiation or depression in synapsis as a result of an injury or a therapeutic intervention [1]. The emergence of non-invasive cortical stimulation techniques such as Transcranial Magnetic Stimulation (TMS) enables the study of neuroplasticity induction in human brain.

Transcranial magnetic stimulation utilizes short high intensity magnetic fields to induce currents that reach the cortex, which depolarize neurons in small regions. This tool has been used for the assessment of corticospinal motor pathway since it can produce a muscle twitch that, in resting muscle, reflects the excitability and local density of the pathway neurons [2].

Likewise, TMS can be utilized in order to potentiate the corticospinal excitability following certain application characteristics related to Hebb principles. Donald Hebb postulated that when two axons of different cells are close enough and repeatedly one taking part in the firing of the other, a growth and metabolic change occurs between them [3]. The application of potentiation protocols of Paired Associative Stimulation (PAS) synchronizes two different stimulus activation, one of them induced by TMS, to converge over the motor cortex. A range of PAS protocols has been developed, combining TMS pulse with different activation stimuli, generating a neuroplasticity response in corticospinal pathway excitability accompanied by the respective changes in function.

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II. Paired Associative Stimulation protocols

A. Peripheral-cortical PAS (pc-PAS),

In the prototypical and original PAS, a single TMS pulse is related with a low-frequency median nerve stimulation, which was applied 25ms before. The nerve stimulation in the hand (Abductor Pollicis Brevis muscle) was applied previously to the TMS in order to have the time to reach the motor cortex for converging with the pulse in the contralateral primary motor cortex (M1)[4]. Repeated pairing of both stimulus over an extended period enhances the excitability of corticospinal projections from M1. Thus, the time of activation is crucial for PAS induced effects, representing the spike-timing dependent plasticity (STDP) form [5]. PAS induced an increase in the amplitudes of the Motor Evoked Potentials (MEPs) in the resting muscle for 30 min and was persistent with a minimum duration of 30–60 min [4] which has been suggested as a representation of Long Term Potentiation (LTP)-like plasticity [6]. In addition, PAS resulted in enhanced motor learning 1 week after its application [7].

B. Cortico-cortical PAS (cc-PAS)

The cc-PAS consists of pairing two TMS single pulse, each applied in a cortical hemisphere. Rizzo et al. designed this PAS version by applying a single TMS pulse over the ipsilateral hand-M1 followed by another single TMS pulse over the contralateral hand-M1 at a constant Inter-Stimulus Interval (ISI) of 8 ms [8]. Their hypothesis was that the propagation of the volley in transcallosal axons could cause a trans-synaptic excitation of specific interneurons in the contralateral hand motor cortex. Koganemaru et al. applied this paradigm and recalled it as Paired Bihemispheric Stimulation (PBS), inducing a PAS protocol with an ISI of 15ms [9].

When the left hand-M1 was stimulated previously to right hemisphere (left-to-right cc-PAS), left-to-right interhemispheric inhibition was attenuated and the corticospinal excitability in the conditioned right M1 was increased. Besides, cc-PAS speeded responses with the left but not right index finger during a simple Reaction Time (RT) task. Symmetrically, right-to-left cc-PAS reduced right-to-left interhemispheric inhibition without increasing corticospinal excitability in left M1. Thus, it is concluded that cc-PAS can induce associative plasticity in interhemispheric

TABLE I
STUDIES REPORTING EXCITABILITY ENHANCEMENT RELATED TO A PAS INTERVENTION

PAS Intervention	Reference	Inter-Stimulus Interval (ISI)	Pairing pulses	PAS Effects
Pc-PAS	Stefan et al. (2000)	25 ms	90 pairings; 0.05 Hz	LTP-like plasticity
	Rajii et al. (2011)	25 ms	180 pairings; 0.1 Hz	Enhanced motor learning
Cc-PAS	Rizzo et al. (2009)	8 ms	90 pairings; 0.05 Hz	Attenuated interhemispheric inhibition; speeded responses; increased corticospinal excitability
	Koganemaru et al. (2009)	15 ms	180 pairings; 0.1 Hz	Facilitated fine finger movements
Movement-related PAS	Thabit et al. (2010)	50 ms	240 pairings; 0.2 Hz	Potentiated corticospinal motor pathway; shortened reaction times

connections between the targeted cortical areas. The efficacy of cc-PAS to induce lasting changes in excitability depends on the exact time of stimuli pairing convergence suggesting an underlying Hebbian mechanism [8] and a STDP kind of plasticity. Fine finger movements were also facilitated by PBS [9].

C. *Movement-related PAS*

As any M1 activation paired with TMS pulse is likely needed for motor pathway potentiation, Thabit et al. chose as an alternative the natural physiological activation of hand-M1 during a RT task. Thus, a new protocol of PAS was designed, by combining TMS cortical activation with a task that requires muscular movement 50ms before, that in turn, through afferent projections, activates M1 as well [10]. This form of PAS induced potentiation in the corticospinal excitability and shortened reaction times in the task that outlasted the stimulation period. This potentiation developed within 20 min, was sustained after intervention and showed associativity. Thus, the characteristics of this change are similar to associative LTP like plasticity. Additionally, this form of induced plasticity was STDP as excitability enhancement was dependent on TMS and the onset of voluntary movement synchronization.

III. CONCLUSION

These findings suggest that TMS interventions have a potential use for improving motor pathway excitability and functional performance applying it following PAS protocols. These improvements are specific to the timing as they respond to cellular synaptic plasticity phenomenon and they induce long term lasting effects, which opens a broad therapeutic work field for more stable changes.

IV. DISCUSSION

As many paired protocols are emerging for the use of TMS in corticospinal excitability potentiation, we believe that eventually, a characterization of each of them will be necessary in order to unveil their strengths and defects.

We suggest a study based on the comparison of these techniques. The comparative relation of excitability enhancement effects and their functional consequences could be tested in the same corticospinal motor pathway, for example in the APB muscle, applying the different protocols that we have reviewed and using comparable parameters, i.e., the equivalent ISI and the same amount of paired pulses at the equal frequency of application.

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Proportional control of FES for grasping using voluntary EMG from stimulated hand muscles

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Abstract— **Currently, functional electrical stimulation (FES) is often applied passively such that preprogrammed stimulation patterns are used. However, passive FES application does not ensure the active participation of individuals voluntarily activating their target muscles, which has been suggested to be important for movement rehabilitation. Here we aim to test the feasibility of a two-channel proportional EMG-controlled active FES (Active FES) system that can augment both hand and wrist flexion and extension by encouraging active participation. Early results show that participants assessed the Active FES system as easy to use, suggesting that it could be implemented as a way to incorporate voluntary muscle activation time-locked and proportional to FES intensity, in order to promote targeted neurorehabilitation of hand and wrist muscles.**

I. Introduction

FUNCTIONAL electrical stimulation (FES) is a widely used technique for passive muscle activation in movement rehabilitation following spinal cord injury and related neurological conditions. In the clinical setting, FES is often applied passively which means that automated stimulation patterns independent of voluntary effort are used. The limitation of this method of FES application is that the active participation of individuals is not encouraged and consequently the cortical drive for voluntary muscle activation is not time-locked with FES. However, it has been hypothesized [1] and evidence suggests [2] that the therapeutic effect of FES is enhanced when it is applied in synchrony with voluntary muscle activation.

One method to encourage voluntary muscle activation with FES is to use a control signal generated from residual electromyogram (EMG) of the FES-stimulated muscle. Residual EMG can then be employed to trigger the onset and/or proportional control of FES intensity. Proportional control is an attractive strategy because it provides more natural control. However, technical problems related to simultaneous recording of EMG and significant electrical noise contamination from the FES makes this control strategy difficult to implement. Recently, single channel proportional EMG has been shown to adequately control FES as an orthotic and rehabilitation technique to promote tenodesis, hand flexion or extension [3,4]. Here we aim to further develop this technique by testing the feasibility of a two-channel proportional EMG-controlled FES system called Active FES for augmentation of finger and wrist flexion and extension to promote targeted active neurorehabilitation of hand and wrist muscles.

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II. Methods

A. Artefact removal

In the Active FES system, EMG was recorded from the extensor digitorum (EDC) and flexor digitorum superficialis (FDS) muscles and then used to control a FES applied to the same pair of muscles. Stimulus artifact recorded with the EMG was eliminated using a comb filter given by

$$x_c(n) = x(n) - bx(n-K), \tag{1}$$

where x_c is the comb-filtered EMG signal, x is the artifact contaminated EMG signal, the coefficient b is a constant and $K = Fs/f$ is the ratio of the EMG sampling frequency and the FES frequency.

Muscle response due to electrical stimulation was removed using an adaptive linear prediction filter assuming that each EMG signal is a band-limited nonstationary, Gaussian noise [5]. The filter is given by

$$y(n) = x_c(n) - \sum_{i=1}^{M} b_i x_c(n-iK)\cdot \tag{2}$$

This filter is similar to (1) but operates by subtracting from the current sample $x_c(n)$, the weighted, using corresponding coefficients b_i, M previous samples separated by K [$x_c(n-iK)$].

The filter in (1) was used first with the filter coefficient $b = 1$ to force the removal of the stimulation artifact. For the adaptive filter in (2), $M = 6$ was used [5] and b_i coefficients were estimated using matrix inversion method implemented in Simulink. The EMG sampling frequency was set to $Fs = 1000Hz$ and the FES sampling frequency was $f = 25Hz$ to give $K = 40 samples/cycle$.

B. *Procedure*

The FES currents were set at a comfortable level for a participant. The set FES currents and the maximum voluntary EMG power were used to calibrate the Active FES system.

Participants were asked to attempt hand and wrist extension and flexion while the magnitudes of the EMGs were extracted and used to proportionally modulated FES intensity by varying the pulse width. In order to verify that the participants could proportionally modulate the intensity of the FES using their EMG signal, they were asked to track a set movement profile presented on the computer monitor by opening and closing the hand and wrist using the Active FES system. The usability of the system was accessed using Quebec User Evaluation of Satisfaction with assistive Technology (QUEST).

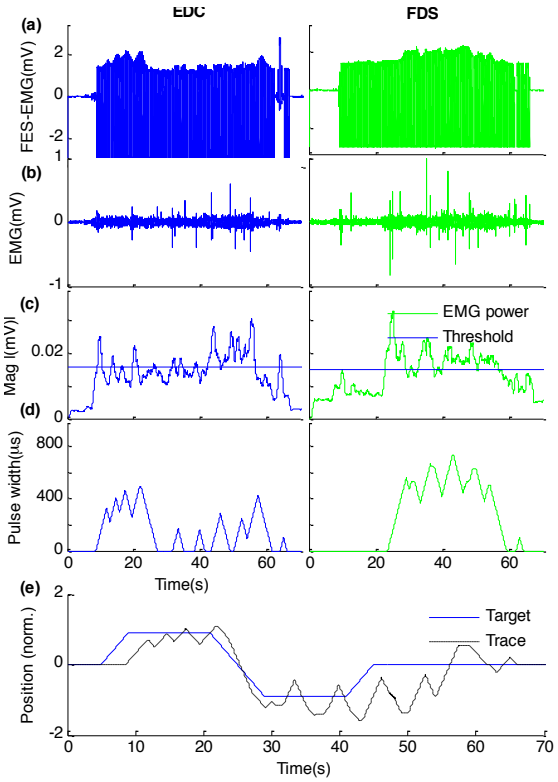

Fig.1. Stimulus artifact-contaminated EMG, extracted EMG, EMG and shape tracing result from participant 1.

III. Results and Discussions

The Active FES system has been tested on two participants with motor incomplete spinal cord injury at the cervical level. Fig. 1 shows a typical result from Participant 1 during the tracking task using the Active FES system. In Fig. 1a the stimulus artifact-contaminated EMG signal was clear as the participant attempted hand/wrist movement. Fig. 1b shows the EMG extracted online from Fig. 1a using the Active FES system. Fig. 1c-d show the corresponding estimated EMG power and FES pulse width modulation. Fig. 1e shows the result of the tracking task.

Although as shown in Fig. 1e, the participant was not able to precisely trace the given shape, he was able to voluntarily control the FES during the session indicating that precise tracking is not required to use the Active FES system. Some of the reasons the participant could not precisely track the shape may be (1) because the participant was not used to receiving FES on a muscle under voluntary contraction, (2) due to possible changes in muscle fibre recruitment during voluntary and varying FES intensity controlled by the target muscle [6] leading to unpredictable variation in voluntary EMG amplitude, and (3) due to changes in background noise level in the extracted EMG because of changes in FES intensity. The first two points may be resolved by the participant practicing and becoming accustomed to the system. The last point requires further investigation, although the noise level changes only when the FES intensity is significantly higher than the calibration value.

Both participants rated the system as easy to use using the QUEST. They were able to voluntarily activate and deactivate the FES and to modulate its intensity using residual EMG elicited during hand/wrist extension and flexion, enabling FES to augment functional hand/wrist opening and closing in a proportional manner.

IV. Conclusion

This early result shows that participants found the Active FES system easy to use, suggesting that it could be implemented as a way to incorporate residual voluntary muscle activation during FES in order to promote targeted neurorehabilitation of specific extensor and flexor muscles. The study is ongoing and further test includes assessing if the Active FES system can enhance wrist range of movement in the patients.

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Motor inhibition elicited by electrical stimulation of afferent pathways and its application in tremor suppression

A. Pascual-Valdunciel*, F.O. Barroso and J.L. Pons

***Abstract*— Spinal reflexes mechanisms have been widely studied in animal models and have proven the contribution of afferent pathways to motor control. Based on these neural circuitry, afferent electrical stimulation has emerged as a promising technique to modulate neuromuscular pathways in several disorders. The aim of this PhD Thesis is to investigate the use of electrical stimulation to evoke afferent inhibition pathways in upper limbs in order to suppress pathological tremor. We will start by exploring different muscle stimulation modalities to elicit inhibition in healthy subjects, aiming to refine or design novel strategies to suppress tremor in patients. Subsequently, the most optimal stimulation strategies to inhibit muscle activity in healthy subjects will be applied in Parkinson's Disease and Essential Tremor Patients aiming to attenuate upper limb tremor. In the future, afferent stimulation as a modulator of motor control at spinal level can potentially be applied as a rehabilitative technique in neural disorders such as pathological tremor.**

I. Introduction

Pathological tremors are involuntary rhythmic movements of one or more body segments. It is the most prevalent movement disorder, hampering activities of daily living (ADL) and leading considerable costs for social and health care systems. Parkinson's Disease (PD) and Essential Tremor (ET) are, among others, the main neurological disorders that produce tremor as a motor symptom [1], [2]. The most extended solution to suppress tremor in ET and PD patients is medication since it interferes directly in the neural tremorogenic mechanisms. However, in most cases, patients become progressively tolerant to drugs and, therefore, need higher doses. Consequently, secondary effects and symptoms increase in time. For these cases, Deep Brain Stimulation (DBS) poses as the most effective treatment, although it holds important drawbacks as well: risk of neurosurgery, surgery costs and tolerance to stimulation. There are few treatment alternatives, with less adverse events and better safety profiles, especially for intractable cases.

An alternative solution is the use of external exoskeletons and prosthesis aiming to mechanically suppress tremor. Yet, these devices are still bulky, interfere with ADL and are limited to home scenarios [3]. Electrical stimulation poses as an attractive approach for tremor suppression, that needs further research. First developments used Functional Electrical Stimulation (FES) to evoke muscle contraction in the tremorogenic muscles and reduce tremor [2], [3]. Two main strategies are applied: 1) co-contraction, which seek increasing the stiffness of the joint by stimulating a pair of antagonist muscles and thus preventing trembling; 2) out-of-phase strategy, which consists in the delivery of electrical stimulation in the antagonist muscles when their agonist present tremorogenic activation. However, FES presents some disadvantages when used for tremor suppression, namely the development of fatigue and discomfort produced by the intensity of stimulation.

In the past five years, neuromuscular stimulation below the motor threshold has emerged as a promising tool for tremor suppression. These strategies seek to stimulate different afferent pathways to produce a modulation at the spinal level by means of interneurons and reflexes circuitries, leading to a reduction of tremor at the muscular output [3], [4]. The mechanisms involved in these tremor suppression strategies haven't been clarified yet, although they overcome common pitfalls of past solutions such as fatigue or interference with voluntary movements.

Some studies proposed that supraspinal along with afferent input at the spinal level are involved in tremor generation [5]. Dideriksen et al. [3] based their studies in this model and applied stimulation below motor threshold to modulate Ia afferent proprioceptive pathways to produce inhibition of antagonist pair of tremorogenic muscles. Other strategies are based on cutaneous afferent pathways. For instance, Hao et al. [6] stimulated the dorsal skin area innervated by the superficial radial nerve to evoke cutaneous reflexes and suppress tremor in PD patients.

Research on spinal reflexes mediated by afferent pathways have been also explored in humans. Mrachacz-Kersting et al. [7] and Nito et al. [8] have shown the inhibitory power of reciprocal and contralateral Ia afferents pathways elicited by electrical stimulation of the nerve in lower an upper limb, respectively. Although these studies were not applied to tremor suppression, they provided novel insights into afferent pathways and the potential of neuromuscular stimulation to modulate motor inhibition.

Based on the state of the art, here briefly described, a set of studies is proposed. Firstly, we aim to evoke motor inhibition in healthy subjects through the modulation of spinal reflexes by means of afferent electrical stimulation. The second study will apply the optimal inhibitory strategy

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found in the first study to suppress tremor in ET and PD patients.

II. Materials and Methods

A two stage research is proposed to optimize motor inhibition elicited by electrical stimulation of afferent pathways and its later application as a tremor suppression strategy, as represented in Figure 1.

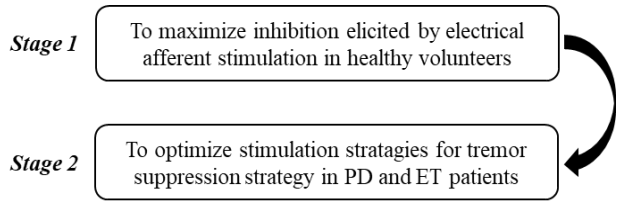

Fig. 1. Scheme of the goals of this research line.

A. To determine motor inhibition in healthy volunteers

The objective of this study is to add novel insight into motor inhibition by exploring different electrical afferent stimulation methods and different spinal reflexes in healthy people. Combination of stimulation of muscles to activate Ia afferent pathways related to the muscle spindle and motor control involved in ipsilateral reciprocal (stretch) reflex and contralateral (withdrawal) reflex in upper limb will be tested. Biphasic stimulation below motor threshold will be applied during isometric voluntary contraction fixed as a percentage of maximum voluntary contraction (MVC). Stimulation duration (single pulse vs multi-pulse) effect on inhibition will be explored. Bipolar surface electromyography (sEMG) and high-density EMG (hdEMG) recordings will be used to characterize muscle activity and inhibition, including information at the motor unit level. Likewise, intramuscular stimulation via thin film electrodes versus surface stimulation will be explored to better determine the afferent fibers involved and the highest inhibitory capability.

B. To optimize tremor suppression strategies

Based on the findings of stage 1, those stimulation protocols that showed greater motor inhibition potential will be applied (and refined) to PD and ET patients suffering from tremor. Bipolar electrical stimulation of the muscle belly will be applied targeting the muscles involved in wrist flexo-extension (flexor carpi radialis and extensor carpi radialis). As performed in stage 1 with healthy volunteers, intramuscular and superficial stimulation will be tested. Out-of-phase stimulation pattern, or continuous stimulation when tremor is detected will be among the strategies explored. Superficial and high-density EMG, as well as inertial measurement systems will be used to record muscle activity and quantify tremor suppression, respectively.

III. Discussion

This contribution to SSNR2018 presents the design and studies to be implemented during a PhD Thesis. First, we briefly present the impact of tremor on patients' quality of life and its social impact; we also summarize the state of the art on tremor suppression strategies and the main drawbacks of the existing solutions. There are evidences supporting the applicability of electrical stimulation below motor threshold as a tremor suppression solution. Notwithstanding, this novel approach needs further research to determine the underlying mechanisms and its maximal potentiality to suppress tremor and become a real alternative to current treatments. The first set of studies here proposed seek to better characterize the effect in muscle activity inhibition of different afferent stimulation strategies in healthy people. Intramuscular stimulation, afferent pathways involved in inhibition and stimulation duration will be the key features explored.

In a second stage, the information extracted about inhibition and the best stimulation protocols will be exploited in PD and ET patients to suppress tremor. Different strategies including intramuscular stimulation and time dependency will be explored and refined on the basis of prior results.

Through this approach, we try to converge the inhibitory effects of stimulation of afferent pathways and its application in the physiology of tremor. Thus, better knowledge on the influence of afferent pathways in motor control, in both healthy and tremor populations, will be acquired. In addition, an optimization of afferent stimulation protocols will be investigated as a novel alternative to current solutions.

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Validation and Repeatability of Online Reflex Activity Measures

Eline Flux, Ronald C. van 't Veld, Jari de Rover, Sanne Ettema, Marjolein M. van der Krogt

Abstract—**Detection of hyperreflexia and intrinsic stiffness in joints is important for neurological patients. Most currently used diagnostic techniques are subjective or lack validity. A system identification (SI) algorithm has recently been developed to online quantify hyperreflexia and intrinsic resistance, which could be used for diagnostics and feedback training. This study assesses the validity and reliability of this SI method. The SI algorithm was applied to twelve participants during control conditions and two conditions known to enhance reflexes: experienced pain and the Jendrassik maneuver. SI outcomes were compared to expected differences as well as to EMG measures to quantify validity and reliability. Validity of SI reflexes is high, as well as within-session repeatability, while repeatability is moderate to good for intrinsic stiffness and validity of intrinsic stiffness was poor. Outcomes support the usability of reflex measures in biofeedback training. For diagnostic purposes, further research should be performed on between-session repeatability and validity of intrinsic stiffness.**

I. Introduction

MANY people with neurological impairments experience increased resistance in joints, e.g. patients with cerebral palsy, spinal cord injury and stroke. Increased joint resistance can lead to increased energy costs in walking [1] and limited muscle growth [2] and is caused by velocity dependent stretch hyperreflexia (increased reflex activity), background muscle activity and/or tissue properties [3]. Measures of hyperreflexia and intrinsic properties are important for clinical decision making and could be used for hyperreflexia down regulation training (e.g. [4]-[5]). However, currently used measures are often subjective or require the use of H-reflexes, which can be painful and is limited in application to superficial muscles. Ludvig et al. [6] developed an online identification (SI) method to quantify reflex activity and intrinsic stiffness, in which intrinsic stiffness is defined as the combined result of background muscle activity and tissue properties. Up till now, this algorithm has only been validated by comparing SI outcomes to EMG outcomes during different muscle activation levels [7]. The aim of this study was to add on the validation of this SI algorithm using two different measures as well as to assess the reliability.

II. Material and Methods

Twelve healthy adults (7 male, 21.3±2.0y) participated in this study. The study was approved by the Scientific and Ethical Review Board of the VU University Amsterdam and written informed consent was obtained from all participants.

Participants were seated in a chair, the Dyno 2.0, with their right foot connected to a single axis actuator by means of a footplate. Perturbations were applied around the ankle joint as specifically designed for the SI algorithm [7].

Measurements started with a control condition (C1) in which participants were asked to remain relaxed to maintain background muscle activity at a constant level. Consequently participants were imposed to two experimental conditions, which are known to facilitate reflexes, in random order. The first condition was experienced pain, as induced by a cold pressor task [8]. Experienced pain was quantified using a visual analogue scale. The second condition was a Jendrassik maneuver (JM) in which participants pulled apart their clenched hands and clamped their jaws [9]. Both conditions were alternated with control conditions (C2 and C3) and each condition was maintained for two minutes.

Reflex activity and intrinsic resistance were estimated according to a modified version of the SI algorithm as described previously [7], using measured torque and position, and averaged over the last 90 seconds for each condition. Muscle activity of the m. gastrocnemius lateralis was measured using the Porti EMG system (TMSi, Oldenzaal, the Netherlands) according to Seniam guidelines [10] and ensemble averaged (see Fig. 1), using the dorsiflexion perturbation onset for alignment. EMG reflex activity was calculated as a validation measure for SI reflex activity by averaging peaks in EMG activity between on average 50 and 80 ms after perturbations and subtracting background EMG activity. Background EMG activity was analyzed as a validation measure for intrinsic resistance and was calculated over 40 ms before onset (Fig. 1).

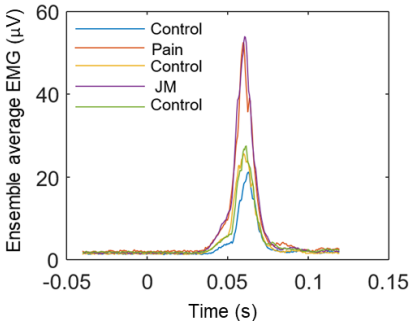

Fig. 1. Example of ensemble averages of the gastrocnemius lateralis for the different conditions of one subject. Dorsiflexion onset is at 0 s.

Validity of SI was analyzed by assessing the Pearson correlation between SI and EMG measures. Furthermore, both pain and JM conditions were compared with all control conditions using paired-sample t-tests to test the response of the measures to conditions known to influence reflex activity and thereby assess the validity. Repeatability of the data between the three control conditions was measured using Pearson correlation coefficients.

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III. Results

TABLE I
CORRELATION COEFFICIENTS

	EMG C1	EMGC2	EMG C3	SI C1	SI C2	SI C3
EMG C1	1	**0.955**	**0.981**	**0.791**	-	-
EMG C2	**0.955**	1	**0.978**	-	**0.837**	-
EMG C3	**0.981**	**0.978**	1	-	-	**0.891**
SI C1	**0.791**	-	-	1	**0.954**	**0.962**
SI C2	-	**0.837**	-	**0.954**	1	**0.941**
SI C3	-	-	**0.891**	**0.962**	**0.941**	1
EMG C1	1	**0.983**	**0.959**	0.394	-	-
EMG C2	**0.983**	1	**0.986**	-	0.525	-
EMG C3	**0.959**	**0.986**	1	-	-	0.436
SI C1	0.394	-	-	1	**0.821**	**0.887**
SI C2	-	0.525	-	**0.821**	1	**0.873**
SI C3	-	-	0.436	**0.887**	**0.874**	1

Top six rows depict reflex measures, bottom six the intrinsic measures. Values in bolt are significant. C1,2,3 reflect the three control conditions.

The two different methods, EMG and SI, showed moderate to high (0.79–0.89) correlations for reflexes and no significant correlations for intrinsic resistance with background activity (Table 1). Participants experienced pain and rated their pain on average 6.8 ± 1.3 out of 10.0. Reflexes were significantly higher during experienced pain and during the JM condition compared to most control conditions, according to both EMG and SI analysis (Fig. 2). During pain conditions, background EMG activity was significantly higher compared to all control conditions, but only significantly higher compared to C1 according to SI analysis. Contrarily, during JM, background EMG activity was only significantly higher compared to C2, whereas it was significantly higher compared to all control conditions according to SI analysis.

Correlation coefficients for the repeatability measure were high for SI reflex activity (0.94–0.96), EMG reflex activity (0.96–0.98), and background EMG activity (0.96–0.99), and moderate to high for SI intrinsic resistance (0.76 – 0.87).

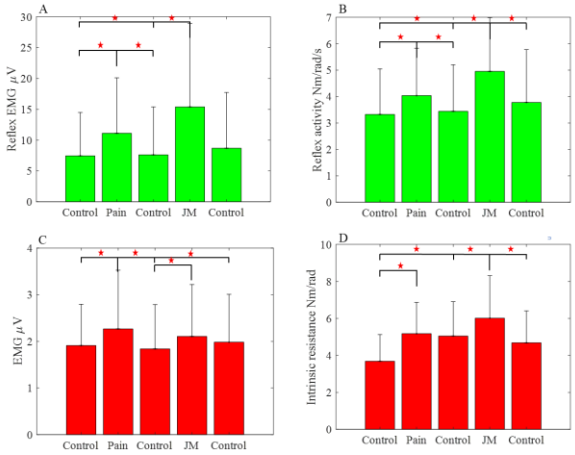

Fig. 2. Overview of all conditions. A depicts EMG reflex activity, B SI reflex activity, C background EMG activity, D SI intrinsic resistance.

IV. Discussion

The online SI algorithm as developed by Ludvig et al. [6] and modified by Van 't Veld et al. [7] appears to be successful in detecting differences in reflex activity due to different experimental conditions. Furthermore, the SI outcomes show a high correlation to reflex measures based on EMG. This further adds to the validation of this method. Additionally, within-session repeatability is high. These results support the use of the online SI hyperreflexia measure in feedback training. Between-session repeatability should be assessed for diagnostic purposes and before SI hyperreflexia can be used as a treatment evaluation method.

Participants showed increased background EMG during the pain condition, but only increased SI compared to C1. SI intrinsic resistance, which is assumed to be the combined result of intrinsic tissue properties and background muscle activity, showed only a moderate to good repeatability and a poor validity according to both validity measures. This is in contrast with previous findings [7], in which multiple background activity levels were assessed and correlations with SI intrinsic resistance were moderate to high. These outcomes do not support the validity to distinct reflex activity and intrinsic stiffness, hence further research should be performed to assess the validity of this measure. This can be done by analyzing conditions that influence the intrinsic stiffness, such as taping to artificially increase intrinsic stiffness. Furthermore, feedback can be given on the background EMG activity to achieve a constant activity level throughout the measurements.

Lastly, it is important to validate both measures in the population of interest, since multiple assumptions are made in the SI which might not apply for the patient population, for example due to smaller electromechanical delay as found in patients with cerebral palsy [11]. Therefore, further research is necessary before it can be implemented in patient specific diagnostics or training.

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Visual Discrimination of Biomimetic Arm Speeds

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***Abstract*— Fine control of robotic prosthetic limbs requires repeatable command signals and comprehensible feedback. However, robotic prostheses currently lack this sensory feedback. Artificial sensory feedback can help users control their prosthesis, but sometimes users choose to rely on vision over this feedback. This suggests that vision can provide the same information as this artificial feedback, but is more trusted. To provide feedback that is not redundant with vision, we should provide information vision cannot provide well. Previous research suggests vision is less precise at estimating speeds than positions. Our work expands this previous knowledge by specifically investigating visual speed perception of biomimetic arm movements. We show that visual uncertainty is greatest when estimating joint speeds, especially when the reference frame speed varies over time. Thus, artificial feedback of joint speed may be more likely to integrate with vision and improve prosthesis control.**

I. Introduction

SENSORY feedback for robotic prosthetic limbs is a research priority for many prosthesis users [1]. Aside from modern research devices, prostheses are not capable of directly replacing the missing proprioceptive information of the state of the limb. Thus, prosthesis users visually monitor their prosthesis while in use to restore some of this missing proprioception [2]. Many attempts to provide artificial feedback have been successful while the prosthesis is obscured, but this benefit sometimes diminishes when the prosthesis is in view. This suggests the artificial feedback is providing similar information to vision, but with greater uncertainty, and users therefore choose to rely on vision over artificial feedback [3].

To avoid providing redundant information, artificial feedback should strive to provide information not provided, or provided poorly, by vision. Previous research suggests vision estimates position with high precision [4], but estimates speed with much lower precision [5]. Speed can be defined in several biologically-appropriate reference frames. For example, movement of the elbow can be defined relative to the environment (absolute speed), or the movement of the shoulder (joint speed). However, visual uncertainty associated with these biomimetic arm movements has not been quantified.

In this study, we investigate visual joint speed perception in the context of providing artificial proprioceptive feedback for prosthetic limbs. Subjects participated in a two-alternative forced choice task observing a virtual two-arm link to determine just noticeable difference (JND) thresholds for different types of arm movements. Additionally, we tested how joint speed JND changes as a result from inconsistent reference frame speeds.

II. Methods

A. Setup

Subjects sat in front of a computer monitor and shown a pair of black two-link systems, similar to a top-down view of a shoulder and elbow, with link lengths of 5cm and endcap diameters of 2.1mm (Fig. 1). These were presented for 2 second each, separated by a 1 second pause.

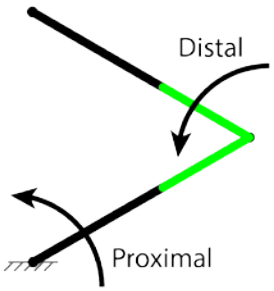

Fig. 1. A two-link system served as the visual stimulus for two-alternative forced choice tasks. In Condition 1, subjects identified which proximal link they perceived was moving faster, and in Condition 2, subjects identified which distal link they perceived was moving faster, relative to the proximal link. In Condition 3, subjects observed the speed of the distal link, but the proximal link moved at different speeds between the two stimuli.

B. Protocol

Subjects completed two-alternative forced choice experiments designed to quantify visual speed discrimination. During a trial, the two-link system was displayed to subjects twice. Three conditions were tested, corresponding to visual discrimination of rotational speeds prosthesis users may experience during daily prosthesis use. For each condition, three nominal speeds were tested: 30 °/s, 60 °/s, and 120 °/s. The starting position of the proximal and distal links were randomized for each stimulus, and the distal link was resampled as needed to prevent it from crossing the proximal link.

The first condition tested visual discrimination of absolute rotational speeds, relative to a static global reference frame (i.e. the screen). During each trial, the proximal link in one stimulus would move at the prescribed nominal speed, and

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in the other stimulus would move at a speed as defined by an adaptive staircase:

$$x(n+1) = x(n) - \frac{C}{n_{shift}+1}[z(n) - \phi]$$

where x was the difference in movement speeds between stimuli, C was the starting speed difference (50%), *nshift* was the number of decision reversals, ϕ was the target JND probability (84%), and z was a Boolean indicator for the subject's decision (z = 1 when correct and z = 0 when incorrect) [6]. This adaptive staircase converged on the 84% JND after 25 decision reversals. The distal link in both stimuli started at 60 °/s and was randomly accelerated and decelerated. Thus, the speed profile was identical between stimuli.

The second condition tested visual discrimination of joint speeds relative to a reference frame (i.e. the proximal link) rotating at consistent speeds between stimuli. During each trial, the distal link in one stimulus would move at the nominal speed (relative to the proximal link), and the other stimulus would move at a speed defined by the adaptive staircase above. The proximal link in both stimuli started at 60 °/s and was randomly accelerated and decelerated. Thus, the speed profile was identical between stimuli.

The third condition tested visual discrimination of joint speeds relative to a reference frame rotating at inconsistent speeds between stimuli. During each trial, the distal link in one stimulus would move at the nominal speed (relative to the proximal link), and the other stimulus would move at a speed defined by the adaptive staircase above. The proximal link in one trial moved at a constant speed of 60 °/s in one trial, and a constant speed of 120 °/s in the other trial.

C. Data Analysis

The 84% JND obtained from each experiment was converted into uncertainty (i.e. standard deviation) of the underlying estimator by dividing by √2 [7]. This uncertainty was then normalized and used as the outcome metric for the results presented in Fig. 2.

III. Results

Visual uncertainty was lowest when assessing the speed of the proximal link, ranging between 20% and 30% (Fig. 2). Visual uncertainty increased when subjects assessed the speed of the distal link relative to the proximal link, with uncertainty ranging between 30% and 50%. When the speed of the proximal link was inconsistent between stimuli, distal link uncertainty tended to increase further, but this increase was not significant. Across all conditions, uncertainty was highest when assessing slow nominal speeds. This trend is particularly prevalent during distal link assessments; at the slowest nominal speed, the distal link being assessed is moving half as fast as the proximal link.

IV. Discussion

Given two sources of information, humans make a single estimate by integrating the two sources, weighted by their uncertainty [3]. Thus, they rely more heavily on the source with lowest uncertainty. Therefore, to suitably replace a missing source of biological feedback with artificial sensory feedback, this feedback should have similar or lower uncertainty than remaining senses, notably vision.

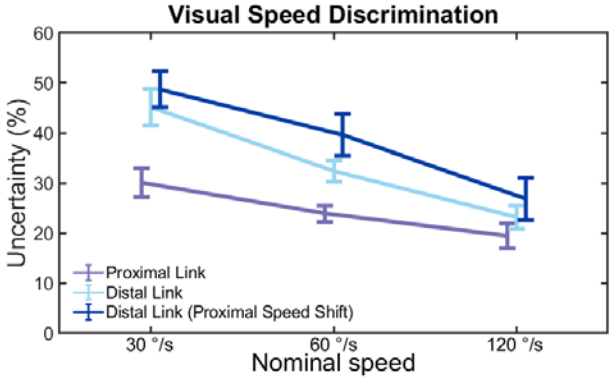

Fig. 2. Uncertainty for visual speed discrimination of the proximal link was between 20% and 30%, while uncertainty for visual speed discrimination of the distal link was between 30% and 50%.

In the context of providing feedback for prosthetic limbs, our results suggest providing proprioceptive feedback in terms of joint speeds defined relative to more proximal body segments, as opposed to absolute speeds defined relative to the torso or the environment. Because of the greater uncertainty associated with visually estimating the speed of the distal link (i.e. joint speed), artificial feedback providing this information is likely to provide the greatest improvement to restoring limb proprioception. This improvement may increase further as the speed of the reference frame increases (e.g. proprioception of elbow movement as the shoulder is in motion). We aim to develop a feedback system which improves joint speed perception and integrates meaningfully with vision, which may lead to and improved sense of proprioception and embodiment of prosthetic limbs and improved control during daily tasks.

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On the Impact of Witnesses Selection in Pulse-to-Noise Ratio Based Assessment of Motor Unit Identification Accuracy from High-Density EMG

F. Urh, A. Holobar

***Abstract*— In our previous studies, we introduced a novel method for accuracy assessment of individual motor unit (MU) firing, identified from high-density surface electromyograms (hdEMG) by Convolution Kernel Compensation (CKC) method. The method is based on previously introduced Pulse-to-Noise Ratio (PNR) and uses pre-identified MU spikes, which we call witnesses, to assess accuracy of other tested spikes. We already tested the method with different number of witnesses, but until now, we selected these witnesses from the true positive (TP) firings only. Such a selection is not possible in experimental condition, where the ground truth about the MU firing is not known. In this study, we tested three different witness selection strategies on hdEMG signals, generated from experimentally recorded MU action potentials from biceps brachii muscle and synthetic MU firing patterns. In the first strategy, witnesses were selected randomly from spikes identified by CKC. In the other two strategies, spikes with maximum or minimum height were used as witnesses, respectively. Maximum spike height selection strategy yielded superior sensitivity in discriminating TPs from hdEMG decomposition errors.**

I. Introduction

In recent years, many new methods for decomposition of high-density electromyograms (hdEMG) and motor unit (MU) firings identification have been proposed [1, 5]. As these methods are non-invasive, they are suitable for use in many applications. But, firstly, accuracy of these methods must be rigorously accessed. One of techniques for accuracy assessment is based on Pulse-to-Noise Ratio (PNR) [4]. This technique is computationally efficient, correlates well with the accuracy of MU firing identification [4] and can be, in contrast to more established two-source technique [8], computed for every identified MU.

Convolution Kernel Compensation (CKC) method iteratively builds a MU filter and then identifies MU spike train by applying this filter to hdEMG. In our previous works [6, 7], we showed that inclusion of a single MU spike in MU filter estimation significantly alters the height of other spikes and, consequently, the PNR of identified MU spike train. In particular, when included in MU filter estimation, true positive firings (TPs) contribute significantly higher values to PNR than false positives (FPs). Therefore, carefully selected pre-identified MU spikes can serve as witnesses of identification accuracy of each next identified MU spike. This significantly extends the state-of-the-art in hdEMG decomposition accuracy estimation, offering the capability of assessing the accuracy of each individual MU firing. However, in our previous work [6, 7], we selected witnesses from 10 to 100 TPs only. Therefore, our initial selection of witnesses was not blind and was not suitable for experimental conditions, where the ground truth about the MU firings is not a priori known. In this study, we propose a new witness selection strategy.

II. Witnesses Selection Strategies

In CKC [3], individual MU spike train is estimated as:

$$\hat{t}_j(n) = \sum_p \boldsymbol{y}(p)^T \mathbf{C}_{\boldsymbol{y}}^{-1} \boldsymbol{y}(n), \quad (1)$$

where p stands for time moments of the estimated *j*-th MU firings, $\boldsymbol{y}(n)$ denotes the vector of the *n*-th sample of all the hdEMG channels and $\mathbf{C}_{\boldsymbol{y}}^{-1}$ is the inverse of correlation matrix of hdEMG channels. Afterwards, PNR may be calculated for $\hat{t}_j(n)$ as proposed in [4]. In [6, 7], we showed that inclusion of a single FP firing in (1) significantly decreases the PNR of $\hat{t}_j(n)$, given that the other MU firings in (1), so called witnesses, come from TPs only [6,7].

In this study, we selected witnesses with one of the following strategies: a) select all the witnesses from TPs only as in [6, 7]; b) select the witnesses randomly from all the spikes identified by CKC (i.e., TPs and FPs combined into a group of witnesses in a random fashion), c) and d) select the witnesses from identified spikes in $\hat{t}_j(n)$ with maximum and minimum height, respectively.

For evaluation purposes, experimentally determined MU action potentials (MUAPs) from the hdEMG of biceps brachii were convolved with predetermined MU firing patterns as in [2]. We simulated 10 seconds long constant 10 % muscle excitation. The signals were sampled at 2048 Hz and decomposed with CKC method [3]. Afterwards, TPs and FPs were identified with firing time tolerance set to 0.5 ms [4]. In total, we identified 52 MUs, but we excluded 11 MUs without at least one FP firing from further analysis. For each of the remaining MUs, we performed 10 evaluation runs. In each run, one tested MU firing (either TP or FP) was randomly selected and combined with preselected witnesses to calculate $\hat{t}_j(n)$ in (1). Afterwards, we calculated PNR on witnesses in $\hat{t}_j(n)$. In this way, tested firing was excluded from PNR calculation and was not used as a witness of its own accuracy. We evaluated the performance of each witness selection

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strategy by comparing the PNR values with FPs included ($PNR_{witnesses+FP}$) and excluded ($PNR_{witnesses}$) from calculation in (1). The number of FPs selected by each tested witness selection strategy was also assessed.

III. Results

The results are exemplified in Figs. 1 and 2 and summarized in Table I.

TABLE I
PNR (MEAN ± STD), NO. OF SELECTED FPS AND NO. OF CASES WITH NONSIGNIFICANT DIFFERENCES BETWEEN $PNR_{witnesses+FP}$ AND $PNR_{witnesses}$ AS DETERMINED BY WILCOXON TEST FOR DIFFERENT WITNESS SELECTION STRATEGIES.

No. of witnesses	10	20	50	100
$PNR_{witnesses+FPs}$ (dB) [6,7]	36.8 ± 1.3	34.4 ± 0.7	32.0 ± 0.2	29.9 ± 0.1
$PNR_{witnesses+FPs}$ (dB) [rand]	39.3 ± 0.6	36.2 ± 0.6	32.0 ± 0.2	30.2 ± 0.1
$PNR_{witnesses+FPs}$ (dB) [max]	39.4 ± 0.2	35.5 ± 0.1	30.8 ± 0.1	27.5 ± 0.0
$PNR_{witnesses+FPs}$ (dB) [min]	38.8 ± 1.0	33.8 ± 0.6	27.7 ± 0.2	25.1 ± 0.1
$PNR_{witnesses}$ (dB) [6,7]	39.9 ± 0.0	35.8 ± 0.0	32.4 ± 0.0	30.1 ± 0.0
$PNR_{witnesses}$ (dB) [rand]	39.8 ± 0.0	36.5 ± 0.0	32.1 ± 0.0	30.3 ± 0.0
$PNR_{witnesses}$ (dB) [max]	40.0 ± 0.0	35.7 ± 0.0	30.9 ± 0.0	27.5 ± 0.0
$PNR_{witnesses}$ (dB) [min]	38.0 ± 0.0	33.0 ± 0.0	27.3 ± 0.0	25.0 ± 0.0
No. of selected FPs [rand]	0.58 ± 0.78	1.20 ± 1.24	3.00 ± 2.66	5.86 ± 4.56
No. of selected FPs [max]	0.00 ± 0.00	0.00 ± 0.00	0.03 ± 0.22	0.73 ± 1.48
No. of selected FPs [min]	4.28 ± 2.29	6.33 ± 3.48	8.13 ± 5.19	8.56 ± 5.81
No. of nonsig. PNR diff. (%) [6,7]	4	4	4	4
No. of nonsig. PNR diff. (%) [rand]	15	30	30	51
No. of nonsig. PNR diff. (%) [max]	4	4	4	13
No. of nonsig. PNR diff. (%) [min]	59	37	8	39

[max] ([min]) - maximum (minimum) CKC spike height selection; [rand] - random CKC spike selection; [6,7] – selection as proposed in [6, 7].

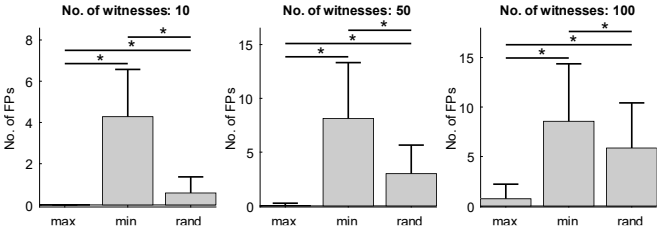

Fig. 1. Average number of FPs in each run, selected by different witnesses selection strategies; max. and min. - maximum and minimum CKC spike height selection; rand. - random CKC spike selection; * - statistically significant difference (Wilcoxon test, $p < 0.05$).

IV. Discussion

Maximum CKC spike height witness selection strategy resulted in higher PNR values and consequently lower absolute difference between $PNR_{witnesses}$ and $PNR_{witnesses+FP}$ than random selection of TPs, proposed in [6, 7]. Nevertheless, the number of FPs, selected by the maximum spike height selection strategy was almost negligibly small (Table I). As a result, the maximum spike height selection strategy shared approximately the same small portion of cases in which the difference between $PNR_{witnesses}$ and $PNR_{witnesses+FP}$ was not statistically significant (about 4%, on average). The other two selection strategies resulted in significantly higher number of FPs in a selected group of witnesses and lower sensitivity of FP detection (Table I).

In conclusion, selection of spikes with maximal height in the MU spike trains, identified by CKC increases the likelihood of TPs in the group of witnesses and increases the sensitivity of the proposed methodology for detection of hdEMG decomposition errors. The methodology is applicable to experimental recordings, but further tests of its sensitivity to different decomposition errors and signal artefacts are still required.

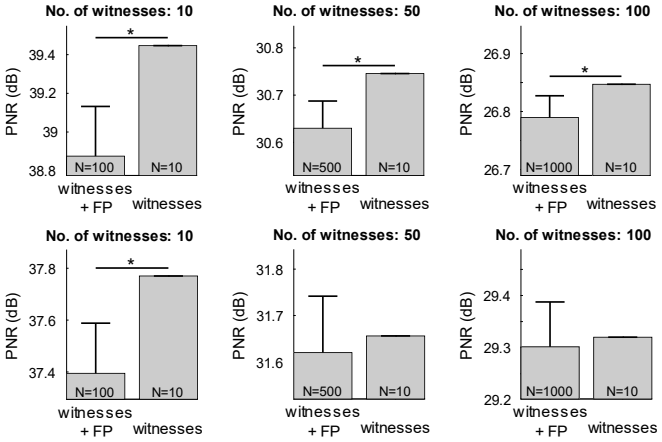

Fig. 2. PNR values (mean ± std) of a representative MU, calculated on different number of witnesses (*left, middle and right plot*) when using maximum CKC spike height (*upper row*) and random CKC spike witness selection strategy (*bottom row*); * - statistically significant difference (Wilcoxon test, $p < 0.05$).

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Design and Control of Lower Limb Exoskeletons for Everyday Life

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***Abstract*—Computer controlled joint units have become state of the art in lower limb exoskeletons, orthoses and prostheses. Ideally the end-user accepts such supportive device as part of his body. Integrating a technical system into the daily life of a human creates challenges regarding robustness, reliability and control of the system. In this contribution an intelligent lower limb orthosis to support activities of daily living for patients with lower limb paralysis is introduced. Data that was obtained in a field test is presented. Results show high load requirements with peak system power up to 5.9 W/kg and a high number of activity cycles with up to 3,720 steps per day. The proposed system is able to handle these stresses; it has proven usability in everyday life.**

I. Introduction

STATE of the art prostheses, orthoses and exoskeletons control motion with computer controlled joint units. In the past few years numerous exoskeletons that restore walking ability for people with complete paralysis have been developed [1], [2]. However, most of these devices are mainly used as rehabilitation and training tools, rather than as daily mobility assist devices, where the end-user ideally accepts his supportive device as part of his body. The uncontrolled environment of home use leads to new design challenges and loading situations that are not yet well known. In this contribution a computer controlled passive orthotic system that supports people with lower limb paralysis in their everyday life is introduced, preliminary usage data obtained in a field study is presented.

II. Materials and Methods

A. Brace System

For this study a prototype version of the C-Brace® system (Ottobock, Duderstadt, Germany) was used. The C-Brace® is a microprocessor controlled knee ankle foot orthosis (mpKAFO, cf. Fig. 1). To control the patient's motion, knee joint compliance is modified by a hydraulic damper which is controlled by servo valves. The knee joint is a fully integrated unit which contains a microcontroller, sensors to measure joint angle and hydraulic force, an inertial measurement unit with 3-axis accelerometer and 3-axis gyroscope, a 32 GB SD card for data logging, a real time clock, a dual mode Bluetooth module and a 3.3V Li-Ion battery. To achieve a good anatomic fit, the interface parts to the patient are custom made out of carbon fiber composites. The patient's leg is fixed in this structure with velcro straps.

B. System Control

To achieve patient acceptance, system control must be intuitive. Therefore, the user should be the highest control entity of the system. In the C-Brace® system, the user controls the system by moving the ground reaction force (GRF) via shifting the center of mass (COM). The knee joint detects this shift in GRF with internal sensors. The valves of the hydraulic damper that control knee joint compliance are then set according to commands generated by a state machine.

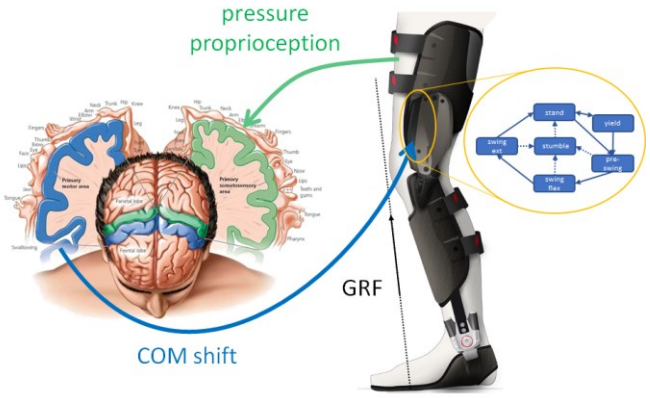

Fig. 1. System overview and control scheme; the brain of the user generates commands to shift the COM and move the GRF vector. The brace system provides resistance according to commands from a state machine and gives feedback by pressure- and proprioceptive sensation.

The state machine runs on the internal microcontroller with an update rate of 100 Hz during regular walking. As human force control bandwidth is in the order of 20 to 30 Hz [3], the control cycle frequency of 100 Hz can be assumed as real time control. For walking activities, a proven control paradigm from prosthetics [4], [5] was adopted. It is based on the "default stance" principle which means that most of the time the system is in a safe stance phase (STP) mode, providing a high resistance against knee flexion to stabilize the patient. Only if the sensor information implies that the patient wants to perform a swing phase (SWP) during

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walking, knee flexion resistance is reduced to initiate SWP. The brace system does not adapt to different terrain conditions, as this adaption is performed by the user. We assumed that, if the system is reliable and predictable, the user will learn to operate the system. The user's superior sensorimotor capabilities will be used for high-level adaptation to terrain conditions and activities.

C. Clinical Evaluation

To obtain data from patients with lower extremity paralysis, a clinical study was conducted at two sites. The study was approved by the local ethic committees from Universitätsmedizin Göttingen (21/1/17) and the ethics commission of the city of Vienna (16-271-0017). In total 8 subjects were enrolled in the study after providing informed consent. All patients were equipped with a C-Brace® system. After a familiarization phase they were allowed to take the braces home for everyday use. The control software was configured to store sensor information at each control cycle (every 10ms, if the patient is active) on the internal SD card.

D. Data processing

Data from the SD card was analyzed using Matlab R2015b and Microsoft Excel 2016. Knee torque was calculated from hydraulic force and knee angle, based on joint kinematics. Daily extreme values for knee torque, knee power, maximum knee angle, and acceleration of the thigh section were evaluated for each patient. Joint load and power data were normalized for patient weight. Additionally, signal amplitudes were counted and stored as histogram data to gain information about activity cycles.

III. Results

Data from three subjects (age 62 to 74 years, weight 45 to 80 kg, height 149 to 176 cm) suffering from neuromuscular deficits of different severity was analyzed. Dependent on the patient, data was recorded for between 37 and 48 days.

All patients were satisfied with the system functionality and the assistance it provided in their everyday life. System control was perceived intuitive and safe. There were no adverse events. P1 wore the braces on 35 out of 37 days, P2 wore it daily. P3 only wore it on 35 out of 44 days due to (not device related) medical conditions. Only days when the system was worn were considered for further analysis. Maximum measured normalized power was 5.9 W/kg, maximum normalized knee flexion torque was 1.8 Nm/kg. For detailed results regarding torque and power measurements please refer to [6]. Fig. 2 shows histogram data for average knee angle amplitudes per day. The amplitude range from 10° to 40° is related to standing and stance phase flexion. Knee joint resistance is high in these situations. Knee angle amplitudes between 40° and 70° occur in swing phase during level walking, where knee joint resistance is low. Amplitudes above 70° are related to activities with high knee joint resistance, like ramp or stair descent or sitting down. It can be seen, that P1 was the most active patient with a daily average of 3720 swing phases related to level walking, and 211 knee flexion amplitudes above 70° per day. P1 and P3 perform stance phase flexion during level walking, which explains the high number of amplitudes between 10° and 40°.

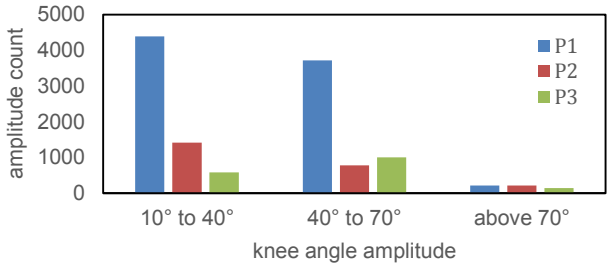

Fig. 2. Histogram of averaged knee angle amplitude counts per day. The colors refer to the different patients.

IV. Discussion

Results show differences in activity cycles between the patients. These differences can be explained with variations in the patient's residual functions and in the individual activity levels. There might even be a correlation between these factors.

V. Conclusion

If a highly functional supportive system is provided to a patient, it will be actually used. This results in high loads and a high number of activity cycles. The control concept with an internal state machine has proven to be safe and effective. The reproducible behavior of the system enabled the user to use the system intuitively in various situations of daily life.

Acknowledgment

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