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Can Passive Mobilization Provide Clinically-Relevant Brain Stimulation? A Pilot EEG and NIRS Study on Healthy Subjects*

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Abstract— **Lower limb rehabilitation is a fundamental part of post-acute care in neurological disease. Early commencement of active workout is often prevented by paresis, thus physical treatment may be delayed until patients regain some voluntary command of their muscles. Passive mobilization of the affected joints is mostly delivered in order to safeguard tissue properties and shun circulatory problems. The present paper investigates the potential role of early passive motion in stimulating cortical areas of the brain devoted to the control of the lower limb. An electro-mechanical mobilizer for the ankle joint (Toe-Up!) was implemented utilizing specially-designed shape-memory-alloy-based actuators. This device was constructed to be usable by bedridden subjects. Besides, the slowness and gentleness of the imparted motion, make it suitable for patients in a very early stage of their recovery. The mobilizer underwent technical checks to confirm reliability and passed the required safety tests for electric biomedical devices. Four healthy volunteers took part in the pre-clinical phase of the study. The protocol consisted in measuring of brain activity by EEG and NIRS in four different conditions: rest, active dorsiflexion of the ankle, passive mobilization of the ankle, and assisted motion of the same joint. The acquired data were processed to obtain maps of cortical activation, which were then compared. The measurements collected so far show that there is a similar pattern of activity between active and passive/assisted particularly in the contralateral premotor areas. This result, albeit based on very few observations, might suggest that passive motion provides somatosensory afferences that are processed in a similar manner as for voluntary control. Should this evidence be confirmed by further trials on healthy individuals and neurological patients, it could form a basis for a clinical use of early passive exercise in supporting central functional recovery.**

I. Introduction

Neurological insults, such as stroke, traumatic brain injuries, encephalitis, anoxia, etc., often produce immediate loss of motor abilities and paresis [1]. As a first consequence of this, an individual's functional independence in daily tasks is jeopardized, and rehabilitation programs must be set up in order to support recovery. In many cases, patients' general conditions require them to remain bedridden for several days or weeks. During this time, physical rehabilitation is sometimes deferred, and this delay may substantially last as long as there is no residual capacity to control the limbs voluntarily or to exercise actively. Passive manipulation is prescribed to try and maintain tissue properties sound, prevent reduction in the range of motion and shun circulatory problems. This type of treatment of the distal extremities is provided especially in order to safeguard all opportunities to recover against the insurgence of later sequelae such as the evolution of contracture, hypertone or spasticity [2].

An important question regarding the use of passive mobilization, particularly in the peri-acute paretic phase, is whether it can also positively influence long-term recovery by avoiding deafferentation of the central nervous system. It could be argued that maintaining a quasi-physiological motion of the impaired limb might have an effect in stimulating the brain areas related to the sensorimotor control, prevent learned non-use, and guide functional remapping and healing.

Figure 1. The Toe-Up! device was designed to produce passive mobilization of the ankle joint and is optimized to to be accessible to bedridden patients and support early lower-limb post-acute rehabilitation.

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In consideration of its paramount importance for gait and hence for the general functional independence of a person, it was decided to focus this work on the rehabilitation of the lower limb, and in particular the ankle joint.

The aim of this study is twofold. First, it presents a new electro-mechanical device (named "Toe-Up!" - Fig. 1) for the cyclic dorsiflexion of the ankle joint. This device was specifically designed to be usable by bedridden neurological patients, and suitable for ankle rehabilitation at a very early (acute) stage. The second purpose of this work is to investigate the brain response evoked by means of Toe-Up! as it generates passive mobilization of the lower limb. This part of the study was conducted on healthy subjects. In this manner, in fact, it is possible to compare brain activation patterns during passive mobilization with those characteristic of voluntary movement. Observations obtained from normal individuals will expedite the set up and analysis of future experiments on neurological subjects.

The methods chosen for recording brain activation were electroencephalography (EEG) and Near Infra-Red Spectroscopy (NIRS). This dual methodology should make it possible to study evoked responses both from an electric and a hemodynamic/metabolic standpoint. It is hoped that the validity of corresponding observations captured by both techniques will be strengthened by the difference in the underlying physical origins of the signals.

II. Materials and Methods

A. The Early-Rehabilitation Device for the Ankle Joint

The device presented in this work utilizes a shape memory alloy (SMA) actuator. SMA are particular metallic materials able to recover their shape when heated after large deformations. This feature depends on the microstructural properties of these alloys, which displays martensitic transformations. Heating can be easily achieved by Joule's effect. By connecting a load to a SMA element this can be displaced during shape recovery; so, SMA, by transducing heat into movement, can produce mechanical work and are suitable for the production of solid-state actuators. Our group has already published some work on applications of SMA actuation for the rehabilitation field [3,4]. The present actuator is based on the Ni-Ti alloy and is specifically designed in order to produce a gentle motion of the impaired limb and to adapt better than electric motors to the requirements of the diagnostic instrumentation. In particular, the inner design of the SMA actuator is amagnetic and this feature helps reduce the electric noise, which could affect the recording of biological signals such as EEG and, less dramatically, NIRS. The device is composed of two main parts: the external case houses the SMA actuator and provides support for the leg of the patient sitting or lying in bed; the foot-plate is directly connected to the actuator and moves through an angle of 30°, gently pushing the patient's ankle into dorsiflexion. The converse motion into ankle extension is produced under the influence of foot weight, ankle tissue elastic recovery and with the help of bias springs. The passive movement of the ankle joint into flexion and extension can be repeated for a selectable number of times. The device was made light in order for it to be easily moved as needed, for example to the beds of different patients. The slowness of the movement (approximately 6°/s) was chosen in order not to arouse excessive stretch reflex response, especially from patients with incipient hypertone. Notice, anyway, that this device was designed to preventively treat acute patients that are unlikely to have developed contractures yet. Its purpose is not to substitute the action of a therapist in producing muscular stretch, but rather to maintain limb mobility and cortical stimulation during (flaccid) paresis.

The controller can be used to decide on the duration of each cycle and the number of cycles in a session. Speed cannot be varied significantly. Maximum available torque is approximately 320Ncm.

Toe-Up! underwent technical checks to confirm its reliability, and passed the required safety tests for electric biomedical devices according to Italian regulation (CEI 60601-1 and UNI CEI EN ISO 14971: 2007).

B. Preclinical Study Protocol

Current investigations were conducted on normal subjects and they comprised 4 conditions (Rest, Active, Passive, Assisted). For the Rest condition (5min.) each subject lay still with eyes open and a leg positioned on the leg-rest of the mobilizer. During the Active (5min.) condition, each subject was cued to carry out a voluntary movement of the ankle, alternating 7 seconds of dorsiflexion hold to 30 seconds of relaxation. The following two conditions depend on the use of the Toe-Up! device, set to produce cycles of 30° dorsiflexion in 7s, and relaxation towards plantarflexion in 30s. For the Passive condition (5min.), the mobilizer imparted a continuous passive motion (CPM) to the subject's ankle; meanwhile, the subject was instructed to stay relaxed without moving the ankle voluntarily. For the Assisted condition (5min.), the subject was instructed to follow the CPM, collaborating actively in the dorsiflexion promoted by the device. During the NIRS acquisition, the total recording time for each condition was divided into 4 blocks, and measurement blocks were carried out in mixed order to allow post-processing through General Linear Models (GLM).

C. EEG Measurement Set-Up and Data Processing

Three young adult subjects were examined (aged 22.3±4.2 years, 2 female). EEG (Neuroscan, produced by Compumedics, Charlotte, NC, USA) signals were recorded at 1000 Hz from 64 channels covering the whole scalp. Recording was carried out for all subjects in all conditions. During EEG acquisition, an ECG and 3 EMG channels were also connected to the subject in order to obtain an electrocardiogram, an electrooculogram signal (EOG) and the electric activation of anterior tibialis (TA) and gastrocnemius (GAM), which are the main muscles involved during active and passive exercise of the ankle joint. EEG data were visually inspected for artefact removal and subdivision into dorsiflexion and plantarflexion epochs. Subsequently, they were 2-70 Hz band-pass filtered and de-noised using an ICA-based method. Artifactual components were rejected and independence from the ground electrode was obtained by referring components to the mean. Power Spectral Density of each voxel signal was estimated via standard Welch procedure. Source localization and reconstruction of voxel-

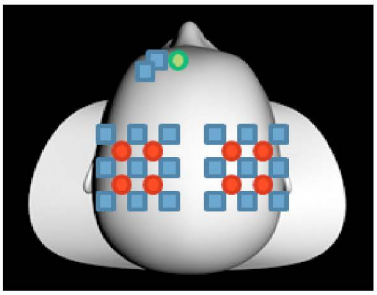

Figure 2. Illustration of NIRS cap design. In this representation, nasion is on top of figure, and inion is at the bottom. Injectors (I) are depicted in red, while receivers (R) are depicted in blue. Frontally, one injetctor for signal quality check (IC) is depicted in green.

wise brain activity was carried out using the sLoreta software, which was also employed for final map Synchronization (ERD/ERS) maps were extracted for standard spectral bands α (8-12 Hz) and β (15-30 Hz).

D. NIRS Measurement Set-Up and Data Processing

Two young adult male subjects (aged 32±7.1 years) took part in the experiment. A commercial NIRS device was used (CE marked). An elastic cap of proper head size was fitted onto the subject's head. The cap had been previously tailored for a 2-set, 32, centered over the motor and somatosensory brain areas. Two additional channels were recorded frontally for signal quality check. Channels were numbered as depicted in Fig. 2. NIRS recordings were carried out at two different wavelengths (760nm and 830nm), in order to probe selectively oxygenated and deoxygenated haemoglobin species (HbO and HHb respectively) in the brain. The location of NIRS channels was calculated as a virtual point midway between the injector and detector positions. NIRS data were visually inspected for artefact removal, and then low pass filtered at 0.030 Hz, so as to preserve the task/rest frequency introduced by the stimulation protocol. Continuous tracks were then segmented into epochs starting at the beginning of each task block, and ending 30 s after the end of the blocks. In doing so, 12 epochs, lasting 90 s each, were extracted. Epochs were first averaged according to the stimulation type, and then grouped, in order to obtain a grand average. Last, GLM was run on the time-continuous data.

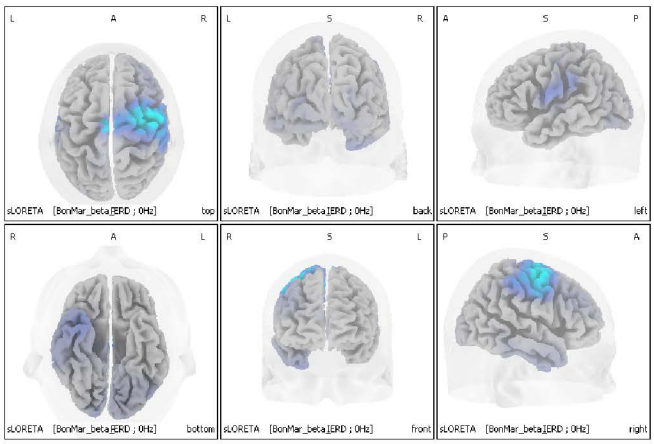

Figure 3. Beta band (15-30Hz) ERD/ERS map for the Passive condition from EEG recording in subject 3, showing activation in the premotor cortex area of the right hemisphere (contralateral to the movement).

Three different regressors, modeling the three different stimulation types, were designed and tested. Activation relating to a particular channel is characterized by the coupling of an increase in oxy-hemoglobin and a decrease in deoxy-hemoglobin for that same channel.

III. Results

A. Performance and Acceptability of the Mobilizer

The tests conducted so far, demonstrated that the Toe-Up! device can produce repeated ankle dorsiflexions in healthy relaxed subjects. The range of motion is partially dependent on individual characteristics of the subjects (foot mass, muscular tone), but is always close to 30°. Movement speed is 6°/s. In spite of this low value, the movement can be perceived very clearly and, to a normal individual, it feels distinctly as a dorsi-plantarflexion. No subject ever reported any discomfort during the use of the Toe-Up! device.

B. EEG

The EEG measurements during the Active condition showed β suppression in primary motor and premotor areas, and in the posterior parietal association cortex. In the Passive condition, desynchronization was observed particularly in the contralateral premotor cortex (Fig. 2 – results on subject 3, as an example), while in the Assisted condition the scenario was intermediate between the Active and Passive ones.

C. NIRS

At least in one case, the NIRS acquisitions clearly captured some activation during the Active condition over the left hemisphere (contralateral to the movement), in the centroparietal area. The activation focus was located in a rather medial position. Passive condition aroused a wide, though weak, pattern of activation in the left centroparietal area. Fig. 3 depicts the results found for subject 1 in the Assisted condition: weak, but more focused, signs of activation can be observed in the same area. Results were interpreted by considering both oxygenated and deoxygenated hemoglobin values, and were later confirmed by GLM analysis, on the basis of the modulus of T-statistics. Subject 2 provided blurrier results, partly due to the darker hair color, which constitutes a barrier for injected light.

D. Statistical Results

Statistical analysis averaging across individuals was not possible so far due to the limited number of subjects.

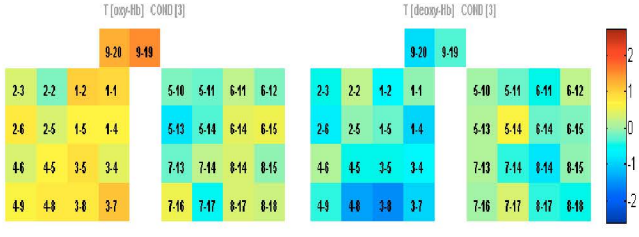

Figure 4. GLM maps for the Assisted Condition using NIRS, in subject 1. Oxygeanted hemoglobin is depicted on the left; deoxygenated hemoglobin on the right. Activation is confirmed when, for a certain channel, oxy-Hb is increased, and *at the same time*, deoxy-Hb is decreased. According to this, signs of activation are observed over the left (contralateral) hemisphere, centroparietally, in both maps (nasion is up, right is right). Statistics for HHb over channel 3/8 provided significance for $p < 0.05$.

IV. Discussion

The results obtained so far demonstrate that the proposed device is reliable, comfortable and easy to use. It produces a

suitable movement of the ankle joint that is clearly recognizable by normal subjects. This is also evident from the fact that in the Assisted condition, EMG signals from the TA and GAM muscles are always temporally related to the dorsiflexion and plantarflexion phases of the device working cycle. It was tried on both right and left sides, and it was verified that there are no differences in comfort when used on either limb. A slight electromagnetic noise was picked-up from the connection to the mains during EEG acquisition, but that was easily and completely removed during band-pass filtering. The SMA actuator itself did not contribute significantly to that noise. This is in line with previous results on the compatibility of SMA actuation and neuroscience instrumentation [6]. No influence on the required quality of EMG signals from the leg muscles was evidenced, although the calf was contacting the leg rest of the mobilizer.

No artifacts were observed on NIRS measurement that are specifically accountable to Toe-Up! device.

Literature reports previous applications of NIRS devices for the study of central motor activation in healthy people and in stroke patients [7-8]. Most papers, however, concentrate on the detection of functional correlates of upper limb motion, and subacute stages of disease. In the present pilot study, NIRS application was further extended to the recording of lower limb correlates in the cortex. Such activity is anatomically expressed in a more medial position with respect to the upper limb region, very near the interhemispheric gap. In spite of this challenging localization, NIRS measurement were carried out successfully.

EEG and NIRS data appear to be mutually consistent, and further bear out observations obtained previously in a magnetoencephalography (MEG) study on a cohort of 11 healthy subjects, with a similar movement protocol for the lower limb [9].

In particular, both sets of data show that the medial centroparietal area reacted during active control, confirming previous anatomical studies [10]. EEG spectra for this condition display most power decrease in the β band.

It is interesting to note that there is a localization of maximum increase in oxy-hemoglobin signal (coupled with a decrease in deoxy-hemoglobin) and desynchronization in EEG activity for the Passive (and Assisted) conditions, approximately in that same part of the cortex as observed for the Active condition, i.e. the contralateral centroparietal area. This region can be identified (Fig. 3) as the premotor cortex, which is an area devoted to motor timing and planning.

From this preliminary evaluation, based on too scant a number of subjects to have general validity, there appears to be a possibility that distal mobilization is processed, to some extent, in a similar way as voluntary control. Should this evidence be confirmed by larger numbers of observations, in particular in neurological patients, it could support the idea that passive mobilization could be used clinically, not only in order to maintain distal tissue properties and limb suppleness, but also to interfere positively in the recovery of central functions, e.g. by avoiding the deafferentation of motor-control structures in the brain during acute paresis.

V. Conclusion

This study suggests that passive mobilization by the Toe-Up! device can produce, besides distal treatment, also cortical stimulation of the brain in the areas devoted to motor programming.

The study is currently in progress. After approval by the appointed Ethical Committee, TBI and stroke patients will be enrolled to test the functioning of the device in a clinical protocol and the cortical response to passive movement in connection to neurological insults.

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