Hybrid Robotic System for Arm Training after stroke: preliminary results of a randomized controlled trial

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***Abstract*—This work presents the preliminary results of a randomized controlled trial aimed at evaluating the efficacy of a novel hybrid robotic system for arm rehabilitation after stroke. The system was developed within the European project RETRAINER and consists of a passive exoskeleton for weight relief combined with an arm EMG-triggered neuroprosthesis. Up to now, 39 patients completed the 9-week intervention: patients in the experimental group achieved a significantly better effect in the motoric outcome measures with respect to control subjects receiving only conventional therapy. These promising results need to be confirmed on a larger sample.**

I. Introduction

ANNUALLY an estimated 5 million people worldwide suffer from stroke [1]. Due to population growth, aging and an increase in the prevalence of risk factors, this number is on the rise [2]. Most stroke survivors are severely limited in performing social and occupational activities, due to impairment, disability and handicap [3]. This is especially true when the upper extremities are affected, where the rate of full recovery is as low as 20% [4].

It is generally accepted that goal-oriented repetitive movement therapy has a positive effect on the recovery of motor functions [5]. Recent studies suggest that the use of Functional Electrical Stimulation (FES) within such a training framework, further improves the therapy outcomes [6].

Within the last years robotic systems [7], [8] and hybrid robotic systems [9] have been tested successfully for the recovery of arm functions.

The herein presented RETRAINER S1 system was designed to train arm functionalities using EMG-triggered FES in combination with a light–weight, passive exoskeleton providing gravity compensation [10]. This work describes the preliminary results of a randomized controlled study (RCT) aimed at testing its efficacy on post-acute stroke patients.

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II. Material and Methods

A. Design and participants

The evaluation of the system was designed as a multi-center single blind RCT conducted at Asklepios Neurologische Klinik Falkenstein (Germany) and at Villa Beretta Rehabilitation Center (Italy). The protocol was registered in ClinicalTrials.gov (NCT03171649).

Patients aged between 18-85 years were considered eligible after experiencing their first stroke two weeks up to nine months before study enrollment. A major unilateral functional impairment, a residual muscular activity in arm and shoulder muscles (MRC ≥1) and a Mini-Mental State Examination >20 were defined as inclusion criteria.

A sample size of 68 patients was a-priori calculated to be capable of detecting a clinically significant between-group difference of 5.7 points in the primary endpoint Action Research Arm Test (ARAT).

B. Interventions

Additionally to their standard therapy, subjects in both groups were trained 30 minutes three times a week for a total of 9 weeks. Whereas subjects of the control group received conventional therapy, subjects of the experimental group used the RETRAINER S1 system for 30 minutes each session. During each session, up to two arm muscles, selected among biceps brachii, triceps brachii and deltoids (anterior, posterior, lateral), could receive FES. The rehabilitative setting enabled the patients to perform 7 different exercises, e.g. anterior reaching and moving objects on a plane or in space, lateral elevation and hand to mouth movements.

C. Outcome Measures and statistical analysis

Patients were assessed before (T0), at the end (T1), and one month after the end of the intervention (T2). The primary outcome measure was the ARAT. Other outcome measures as the Motricity Index (MI), the Motor Activity Log (MAL), the Box&Blocks Test (BBT), and the Stroke Specific Quality of Life Scale (SSQOL) were collected.

A t-test for independent samples was applied to evaluate between-group differences in terms of age and time since stroke.

Linear mixed model analyses for repeated measures (p-value<0.05) were made for each outcome measure, with group and time entered as fixed effects, and the crossover effect of time and group as an interaction term.

III. Results and Discussion

Up to now, a total of 39 patients were recruited for the study and randomized to the experimental (n=19) and the control group (n=20). All patients performed the post-treatment assessment and were included in the analysis.

TABLE I
PARTICIPANTS' CHARACTERISTICS

	Experimental group (N=19)	Control group (N=20)	p-value‡
Age*, years	59.0 (15.9)	67.7 (12.1)	0.06
Time since event*, day	64.3 (66.0)	79.6 (93.8)	0.56
Gender (male / female)	13 / 6	12 / 8	
Etiology (ischemic / hemorrhagic)	6 / 6	10 / 4	
Affected side (left / right)	12 / 7	13 / 7	

* Mean (standard deviation)
‡ t-test for independent samples

Table I shows the participants' characteristic at baseline: no differences were found between group.

Table II reports the changes over time and between groups: a more significant improvement was found for all outcome measures but SSQOL in favor of the experimental group, as highlighted by a p-value<0.05 for the interaction effect. The missing significant improvements in the SSQOL could be attributed to the fact that most surveys have been performed during the inpatient stay of the recruited subjects. Experiences in their familiar environment at home could not be considered.

The significant improvements in the motoric outcome measures in favor of the experimental group might be ascribed to three different factors: the increased afferent feedback provided by FES in close association with the voluntary effort of the patient, the high number of purposeful repetitions in a sufficient amount of time allowed by the system, and the task-specific training which was made by the weight compensation provided by the exoskeleton.

IV. Conclusion

Up to now only half of the sample size has been performed the post treatment assessment and therefore the present results are not statistically powerful. Nevertheless, the preliminary results about the efficacy of the RETRAINER S1 system are promising and indicate a positive effect in the motoric rehabilitation of acute stroke patients. A clinically significant between-group difference in the primary outcome was found at the end of the intervention and preserved after one month, but these results need to be confirmed at the end of the RCT.

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TABLE II
CHANGES OVER TIME AND BETWEEN GROUPS (N=39)

	Group	T0*	T1*	T2*	p-value‡ (group effect)	p-value‡ (time effect)	p-value‡ (group*time effect)
ARAT (0-57)	Control	12.5 (18.1)	17.7 (20.3)	15 (18.6)	0.266	<0.001	0.003
	Experimental	6.2 (12.9)	32.3 (20.2)	27.3 (19.6)			
ARAT gross arm movement (0-9)	Control	3.5 (3)	4.8 (2.4)	3.8 (2.7)	0.587	<0.001	0.008
	Experimental	2.1 (2.3)	6.2 (2.5)	5.2 (2.7)			
MI total (0-100)	Control	39.7 (19.6)	54.6 (16.8)	52.9 (15.6)	0.077	<0.001	0.046
	Experimental	40.8 (15.6)	62.8 (15.4)	67.2 (13.9)			
MI elbow & shoulder (0-66)	Control	28.7 (10)	36.4 (10.9)	35.1 (10.7)	0.137	<0.001	0.046
	Experimental	27.2 (10.1)	42.2 (9.4)	43.2 (9)			
MAL quality (0-5)	Control	0.3 (0.4)	0.9 (0.9)	0.8 (0.9)	0.296	<0.001	0.091
	Experimental	0.2 (0.3)	1.2 (1)	1.5 (1.1)			
MAL quantity (0-5)	Control	0.2 (0.4)	0.8 (0.9)	0.7 (0.8)	0.182	<0.001	0.029
	Experimental	0.1 (0.2)	1.2 (1.1)	1.4 (1)			
BBT	Control	5 (10)	9 (14)	9 (13)	0.106	<0.001	0.003
	Experimental	2 (4)	19 (15)	21 (18)			
SSQOL (49-245)	Control	102 (38)	102 (29)	102 (23)	0.495	0.334	0.838
	Experimental	112 (43)	108 (38)	106 (31)			

*Mean (standard deviation); ‡ Linear mixed model analysis for repeated measures