LA RIABILITAZIONE FUNZIONALE ROBOTICA POST-ICTUS

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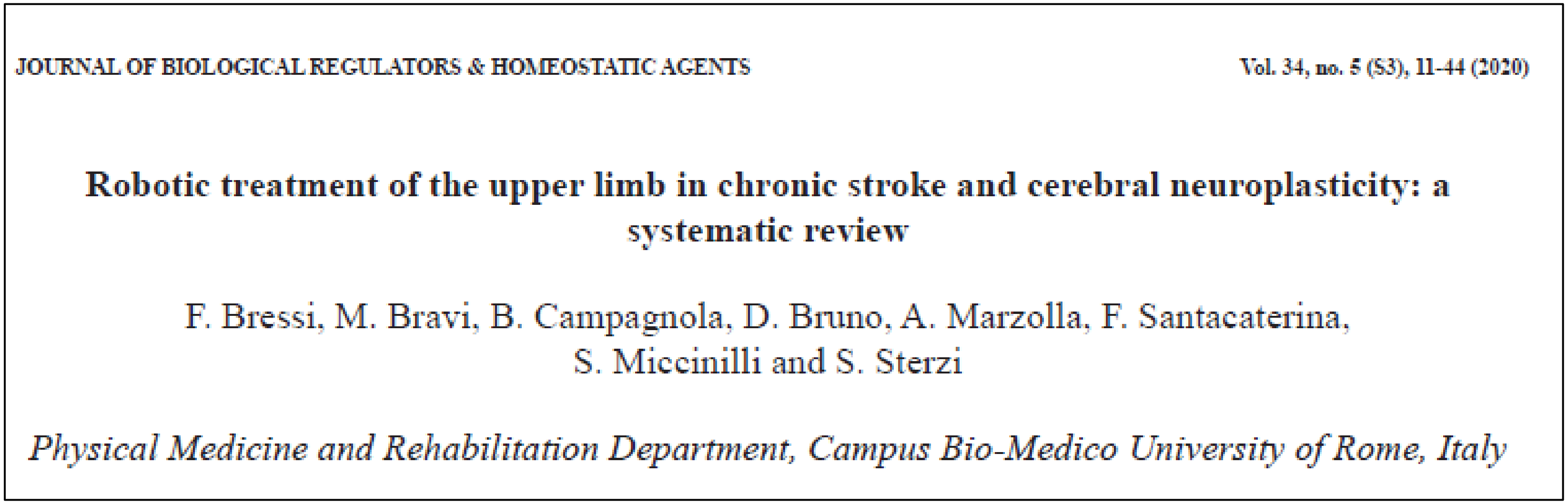
Roma, 15 Giugno 2021



JOURNAL OF BIOLOGICAL REGULATORS & HOMEOSTATIC AGENTS Vol. 34, no. 5 (S3), 11-44 (2020)

Robotic treatment of the upper limb in chronic stroke and cerebral neuroplasticity: a systematic review

F. Bressi, M. Bravi, B. Campagnola, D. Bruno, A. Marzolla, F. Santacaterina,
S. Miccinilli and S. Sterzi

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“Robotic rehabilitation plays a **crucial role** since it allows to perform a repetitive, intensive, and task-oriented treatment, adaptable to the patients’ residual abilities, necessary to facilitate recovery and the rehabilitation of the paretic UL. It has been proposed that robot-mediated training may **amplify neuroplasticity** by providing a major interaction of proprioceptive and/or other sensory inputs with motor outputs, with significant **modifications in functional connectivity** (coherence) within the fronto-parietal networks (inter- and intra-hemispheric functional connectivity) related to processes of movement preparation and execution.

However, the neurophysiological mechanisms underlying this reorganization are not entirely clear yet. Therefore, the aim of this study is to revise the literature, which assesses **the effect of robotic treatment in the recovery of UL deficits measured in terms of neuroplasticity** in patients affected by chronic stroke”.

Nei paesi industrializzati le *principali cause di disabilità* sono rappresentate da alcune patologie neurologiche, quella con maggiore incidenza è lo stroke.

Il miglioramento della funzionalità degli arti superiori e la deambulazione dopo una lesione cerebrale richiedono un *approccio riabilitativo precoce e intensivo*.

Gli studi epidemiologici nei pz con esiti di stroke indicano che, a distanza di 6 mesi dall'evento acuto, dal *30 al 66% dei soggetti colpiti da ictus rimane con un arto superiore non funzionale*, mentre solo nel 5-20% dei casi è dimostrato un recupero più o meno completo della funzionalità.

La *riabilitazione robot-assistita* è sicuramente la tecnologia che a partire dal 1990 ha avuto il maggior sviluppo e ha permesso il trattamento anche di situazioni di disabilità complessa e grave.

Il vantaggio principale dell'applicazione di dispositivi tecnologici è rappresentato dalla possibilità di *programmare e replicare gli interventi e di verificarne l'efficacia*.

Janne M Veerbeek et al, 2016

Laboratorio di Riabilitazione e Robotica

(in coll. con Unità di Ricerca di Robotica Biomedica e Biomicrosistemi) S.Sterzi - E.Guglielmelli

- InMotion^2 Shoulder/Elbow robot
- InMotion^3 Wrist Robot
- BTS SMART SYSTEM (Movement Analysis + OEP)
- Robot Icone
- KUKA Robotic arm for human interaction
- Gloreha Sinfonia

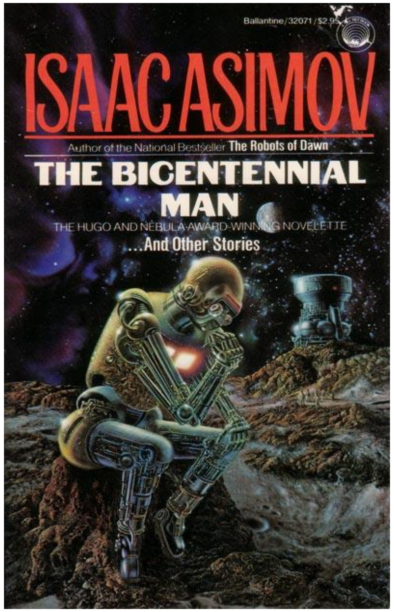
Robotica

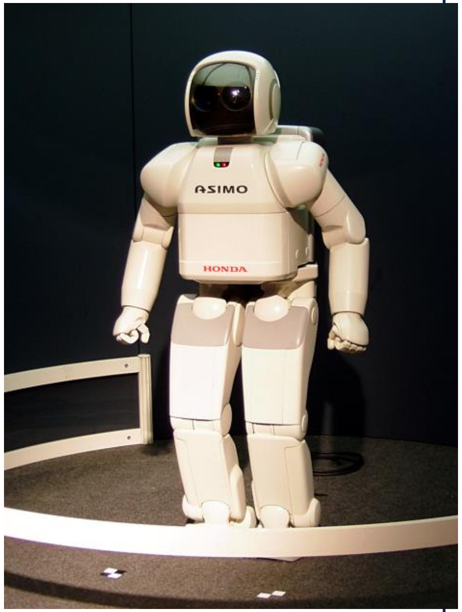
La robotica è una branca dell'ingegneria meccatronica, (studio dell'integrazione tra la meccanica, l'elettronica e l'informatica al fine di introdurre l'automazione per l'ottimizzazione del lavoro umano)

- studia e sviluppa metodi e strumenti per progettare sistemi in grado di generare e controllare movimenti e forze con diversi livelli di autonomia
- in essa confluiscono approcci di molte discipline, dalle scienze cognitive a scienze come la linguistica, la psicologia, la biologia, la fisiologia, l'automazione, l'elettronica, la fisica, l'informatica, la matematica e la meccanica.

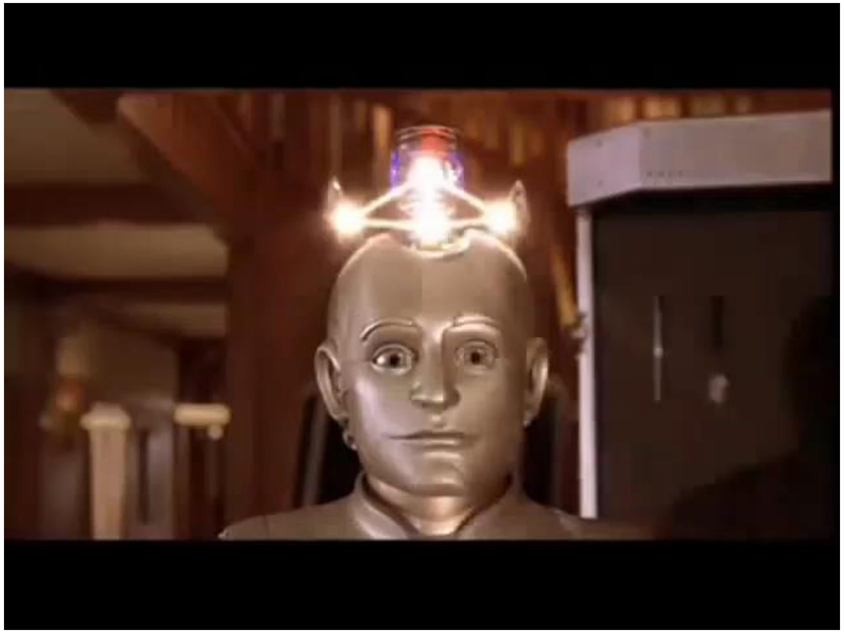
-1950 Primo robot industriale negli Stati Uniti (J.Engelberger).

-1960 Primo robot industriale installato presso un impianto produttivo della General Motors nel New Jersey (USA).





Le origini della robotica moderna



Prima Legge: “Un robot non può recar danno a un essere umano né può permettere che a causa del proprio mancato intervento un essere umano riceva danno”.

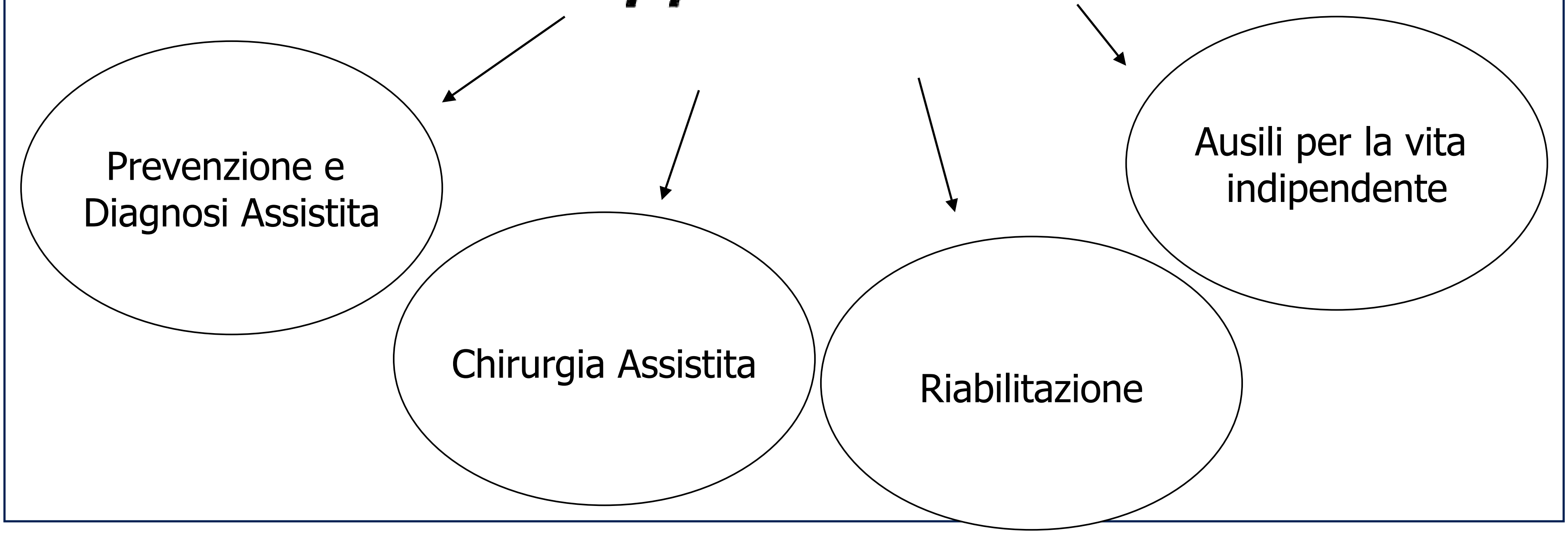
Seconda legge: “Un robot deve obbedire agli ordini impartiti dagli esseri umani purché tali ordini non contravvengano alla prima legge”.

Terza legge: “Un robot deve proteggere la propria esistenza purché questo non contrasti con la prima e la seconda legge”.

Le origini della Robotica Biomedica

Paolo Dario, Eugenio Guglielmelli, Benedetto Allotta and Maria Chiara Carrozza*

Robotics for Medical Applications



Prevenzione e Diagnosi Assistita

Chirurgia Assistita

Riabilitazione

Ausili per la vita indipendente

IEEE Robotics & Automation Magazine, Vol. 3, No. 3, 1996

Definizione di Robot Riabilitativo

Sistema robotico in grado di coadiuvare il terapista nella somministrazione di procedure riabilitative *programmabili e personalizzabili* in funzione

- del tipo di trattamento necessario
- delle abilità residue del paziente valutate prima e durante il percorso riabilitativo

«Inversione del paradigma industriale: la robotica riabilitativa ha storicamente introdotto e sviluppato robot ad elevato grado di interazione con l'uomo»

Caratteristiche del Trattamento Robotico

- ✓ Approccio terapeutico strutturato, ripetitivo ed intensivo
- ✓ Task-oriented
- ✓ Adattabilità e flessibilità: assisted as much as needed
- ✓ Scenari di gioco per aumentare il coinvolgimento: immersive reality
- ✓ Spazio operativo del task 2D/ 3D
- ✓ Monitoraggio e registrazione quantitativa della performance
- ✓ Costruzione e implementazione di database Trials multicentrici

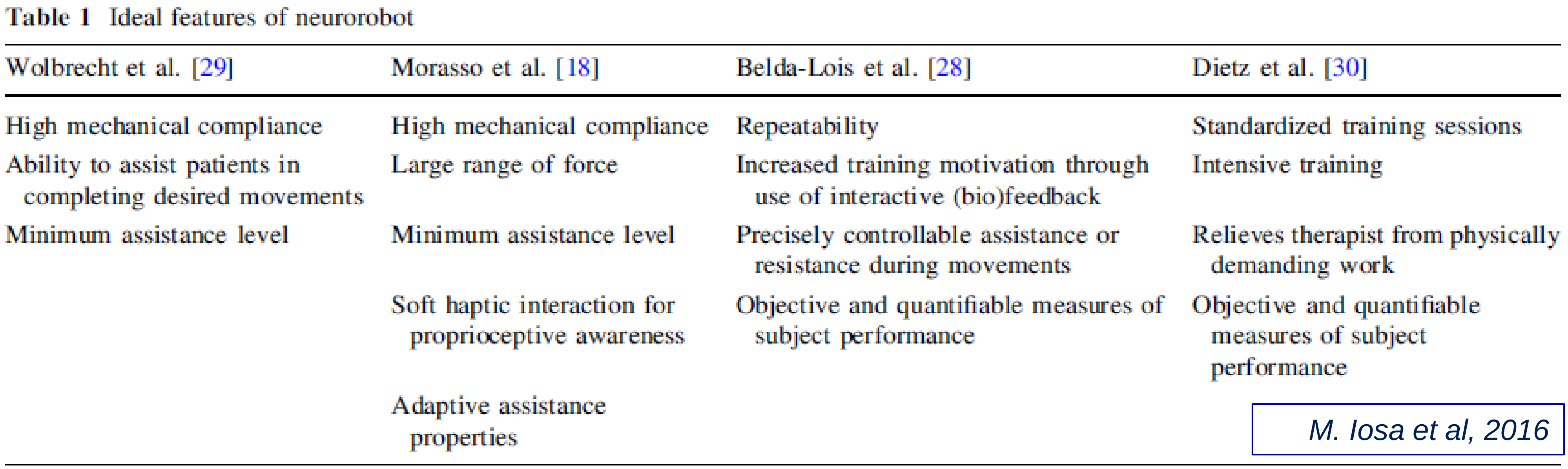
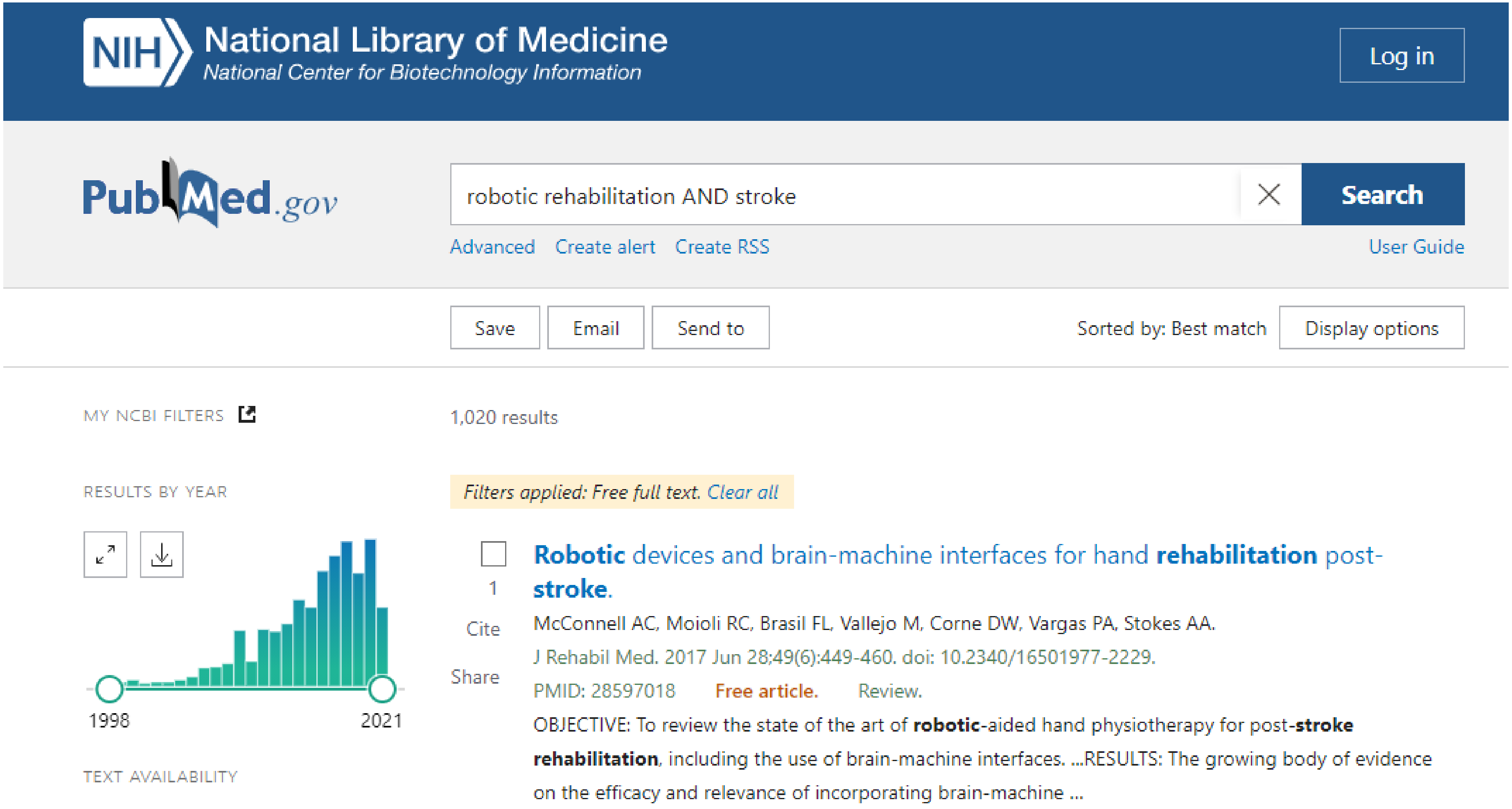


Table 1 Ideal features of neurorobot

Wolbrecht et al. [29]	Morasso et al. [18]	Belda-Lois et al. [28]	Dietz et al. [30]
High mechanical compliance	High mechanical compliance	Repeatability	Standardized training sessions
Ability to assist patients in completing desired movements	Large range of force	Increased training motivation through use of interactive (bio)feedback	Intensive training
Minimum assistance level	Minimum assistance level	Precisely controllable assistance or resistance during movements	Relieves therapist from physically demanding work
	Soft haptic interaction for proprioceptive awareness	Objective and quantifiable measures of subject performance	Objective and quantifiable measures of subject performance
	Adaptive assistance properties		

M. Iosa et al, 2016



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robotic rehabilitation AND stroke ✕ **Search**

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RESULTS BY YEAR

TEXT AVAILABILITY

1,020 results

Filters applied: Free full text. Clear all

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Cite

Share

Robotic devices and brain-machine interfaces for hand **rehabilitation** post-**stroke**.

McConnell AC, Moioli RC, Brasil FL, Vallejo M, Corne DW, Vargas PA, Stokes AA.

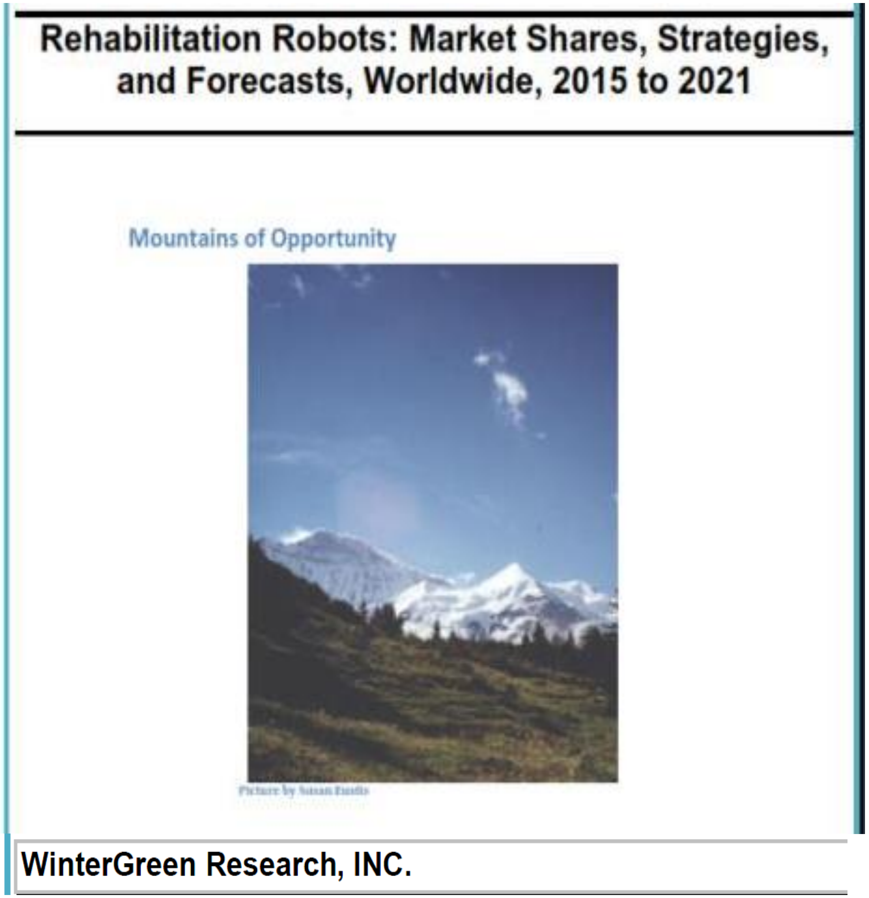
J Rehabil Med. 2017 Jun 28;49(6):449-460. doi: 10.2340/16501977-2229.

PMID: 28597018 Free article. Review.

OBJECTIVE: To review the state of the art of **robotic**-aided hand physiotherapy for post-**stroke** **rehabilitation**, including the use of brain-machine interfaces. ...RESULTS: The growing body of evidence on the efficacy and relevance of incorporating brain-machine ...

Crescita mercato dei robot riabilitativi

"….Rehabilitation robot market size at $43.3 million is expected grow dramatically to reach $1.8 billion by 2020."



Rehabilitation Robots: Market Shares, Strategies, and Forecasts, Worldwide, 2015 to 2021

Mountains of Opportunity

WinterGreen Research, INC.

Classificazione dei Robot Riabilitativi

1-Robot per il recupero della funzionalità fisica, sociale, comunicativa e cognitiva *

- Operativi o cartesiani
- Esoscheletri/indossabili
- Non contact

2-Robot per assistenza/ausili di persone con disabilità cronica nello svolgimento delle ADL

3-Protesi robotiche

*Therapy robots generally involve at least two persons simultaneously: person with a disability who is receiving the therapy and therapist who sets up and monitors the interaction with the robot (the disabled person's caregivers) .

Robot operativi (end-effector-based)

Gait Trainer I

Il contatto fra la struttura meccanica ed il paziente è limitato all'effettore a cui il soggetto è collegato tramite apposita interfaccia.

Vantaggi:

a) Possono essere disegnati utilizzando componenti standard o robot;
b) Possono essere programmati facilmente nello spazio cartesiano da utilizzatori non esperti

Svantaggi.

a) Non riescono ad assistere ciascuna articolazione singolarmente in maniera indipendente;
b) Il paziente deve avere conservato un livello minimo di sinergia motoria residua per coordinare il movimento poliarticolare per riprodurre l'esercizio terapeutico richiesto.

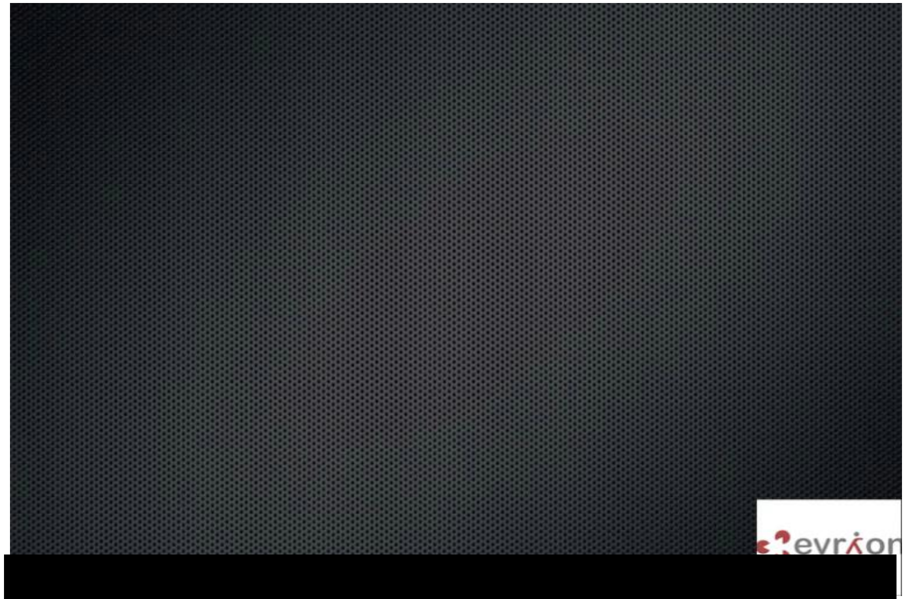
Robot esoscheletrici

Nella maggior parte dei casi si utilizza una struttura cinematica esoscheletrica biomimetica.

Esoscheletri, indossabili, eseguono lo stesso tipo di movimento svolto dal paziente e nei quali l'interfaccia uomo-macchina è estesa a tutto l'arto o alla parte di interesse clinico.

Il numero di gradi di libertà è uguale a quello delle articolazioni sulle quali il trattamento ha l'obiettivo di intervenire.

Robot esoscheletrici



Vantaggi:

- ✓ Controllo indipendente dei singoli giunti articolari
- ✓ Controllo delle differenti sinergie

Svantaggi.

- ✓ Complessità funzionale e tecnica (cinematismo adatto a generare il movimento associato ai centri di rotazione interni al corpo umano)
- ✓ Progettazione accurata per soddisfare i requisiti antropometrici e cinematici (possibili malallineamenti tra robot e articolazioni)
- ✓ Invasività per il paziente in termini di peso, dimensioni e indossabilità

Robot non contact

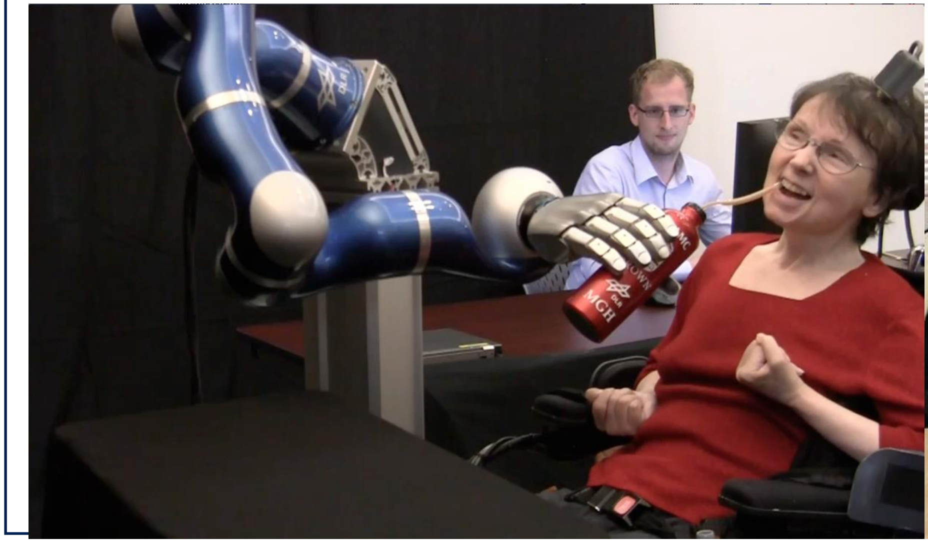
Socially Assistive Robot (SAR):

sistemi sviluppati per motivare e allenare i soggetti in semplici attività fisiche.

Robot per l’assistenza

Promuovono l’autonomia dei disabili e anziani, realizzati per uso domestico e per durare a lungo, adattati alle preferenze dell’utilizzatore finale

- Manipolazione
- Mobilità
- Cognitivo



Robot per l’assistenza

“*The studies demonstrate that a person with chronic tetraplegia can perform consistent, natural, and complex movements with an anthropomorphic robotic arm to regain clinically significant function.*”
Lancet 2013

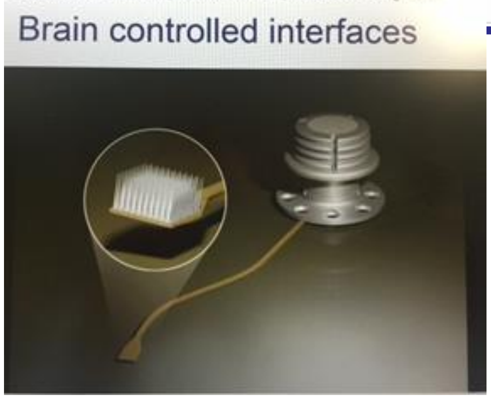
I segnali ECoG sono stati prelevati da pazienti tetraplegici ed utilizzati per controllare un sistema robotico braccio-mano.

Shared control of multi-fingered robotic hand prostheses – E.Guglielmelli

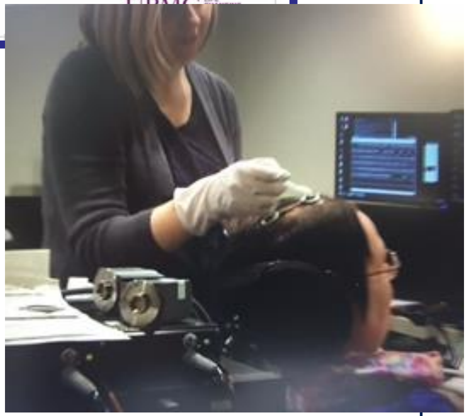
Brain controlled interfaces

One Small Nibble One Giant Bite

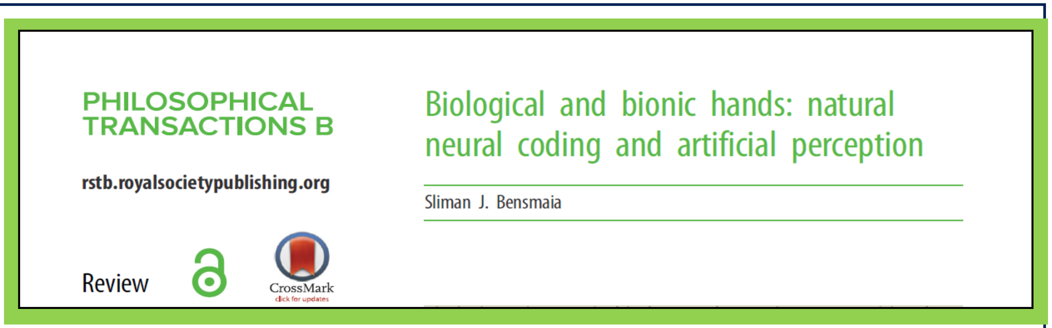
The University of Pittsburgh School of Medicine
and UPMC Rehabilitation Institute
Brain Computer Interface Trial - Intracortical Arrays



Brain controlled interfaces



Protesi Robotiche


PHILOSOPHICAL TRANSACTIONS B

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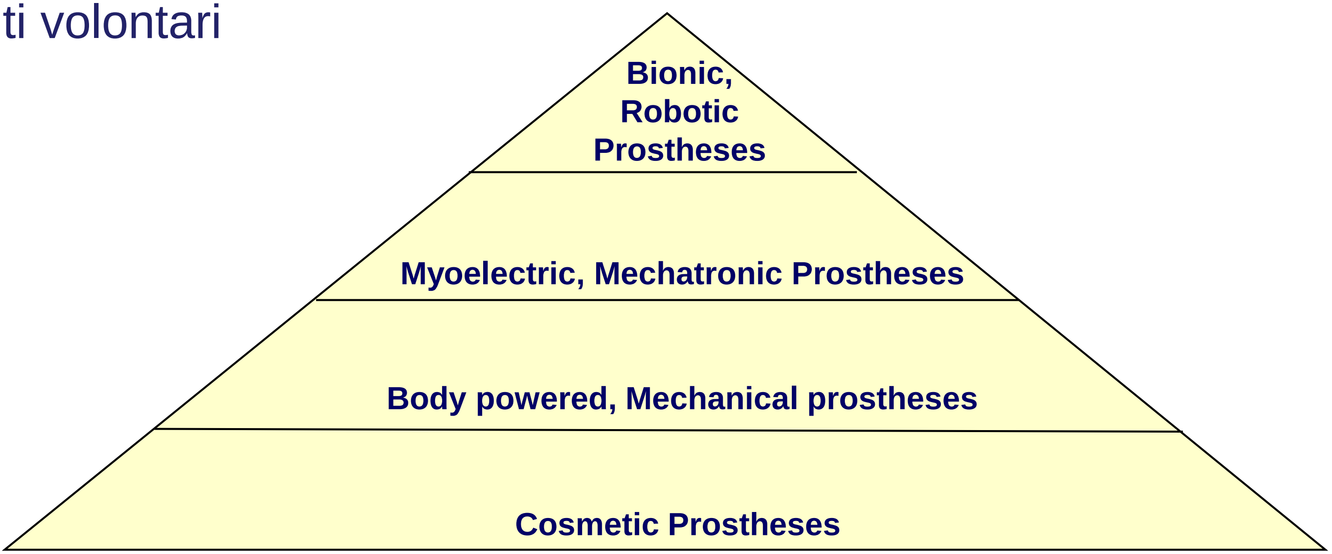
Review

Biological and bionic hands: natural neural coding and artificial perception

Sliman J. Bensmaia

Due principali innovazioni in neuroprotesica:

- lo sviluppo di una protesi robotica antropomorfa che riproduca la maggior parte delle funzioni di un braccio umano
- la ridefinizione degli algoritmi che decodifichino le attività cerebrali per replicare i movimenti volontari


Bionic, Robotic Prostheses

Myoelectric, Mechatronic Prostheses

Body powered, Mechanical prostheses

Cosmetic Prostheses

End-Users as Percentage of the Target Population

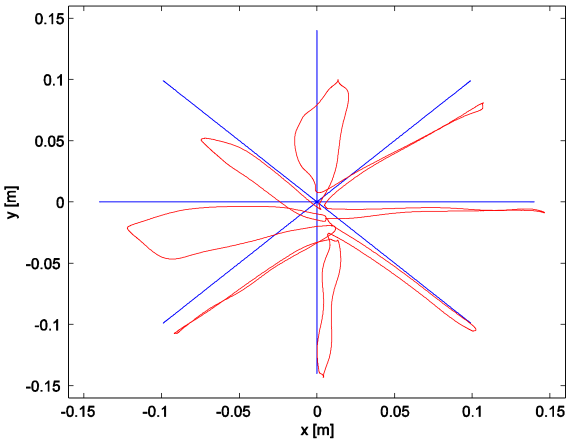
Indicatori di Performance Quantitativi

Indici Cinematici:

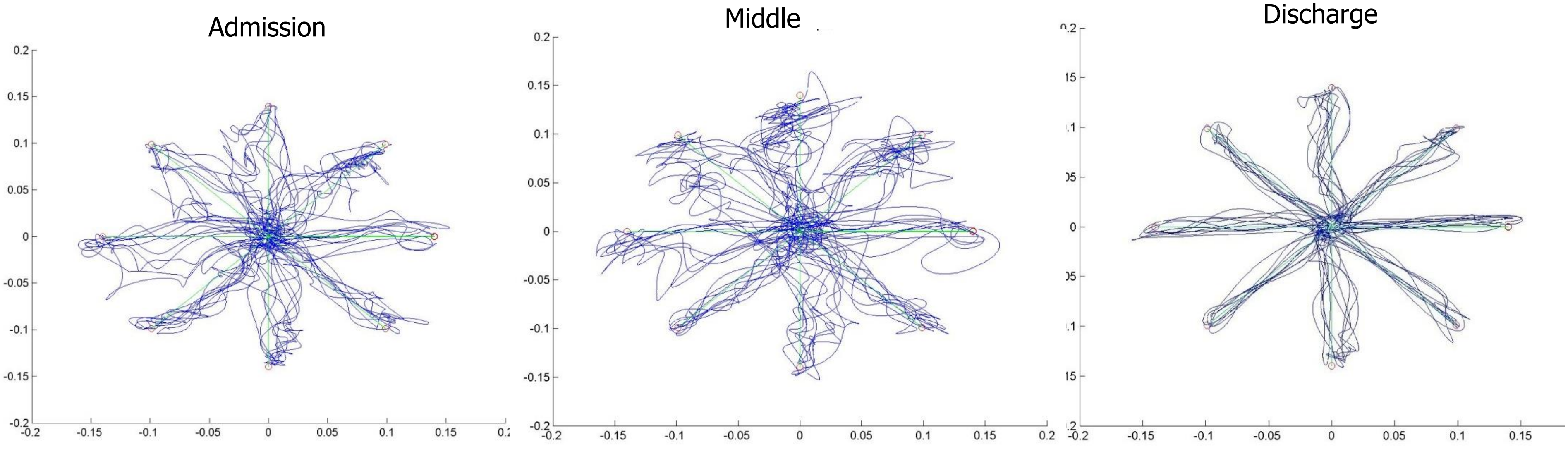
vengono registrati la posizione e la velocità nello spazio cartesiano durante il moto e vengono calcolati offline indicatori quantitativi sulle caratteristiche spaziali e temporali del recupero delle capacità motorie

Indici Dinamici:

misurano le forze applicate durante il moto e il lavoro speso durante l'esecuzione dell'esercizio motorio



Posizione cartesiana ideale (in blue) ed effettiva (in red)

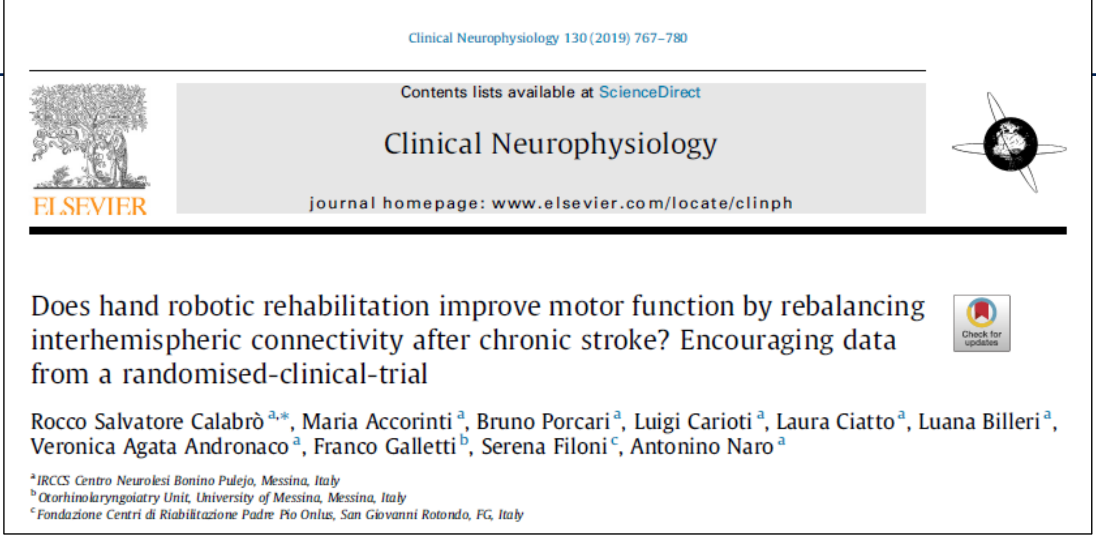


Admission

Middle

Discharge

Patient time course



Clinical Neurophysiology 130 (2019) 767–780

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Does hand robotic rehabilitation improve motor function by rebalancing interhemispheric connectivity after chronic stroke? Encouraging data from a randomised-clinical-trial

Rocco Salvatore Calabrò [a,*], Maria Accorinti [a], Bruno Porcari [a], Luigi Carioti [a], Laura Ciatto [a], Luana Billeri [a], Veronica Agata Andronaco [a], Franco Galletti [b], Serena Filoni [c], Antonino Naro [a]

[a] IRCCS Centro Neurolesi Bonino Pulejo, Messina, Italy
[b] Otorhinolaryngoiatry Unit, University of Messina, Messina, Italy
[c] Fondazione Centri di Riabilitazione Padre Pio Onlus, San Giovanni Rotondo, FG, Italy

ABSTRACT

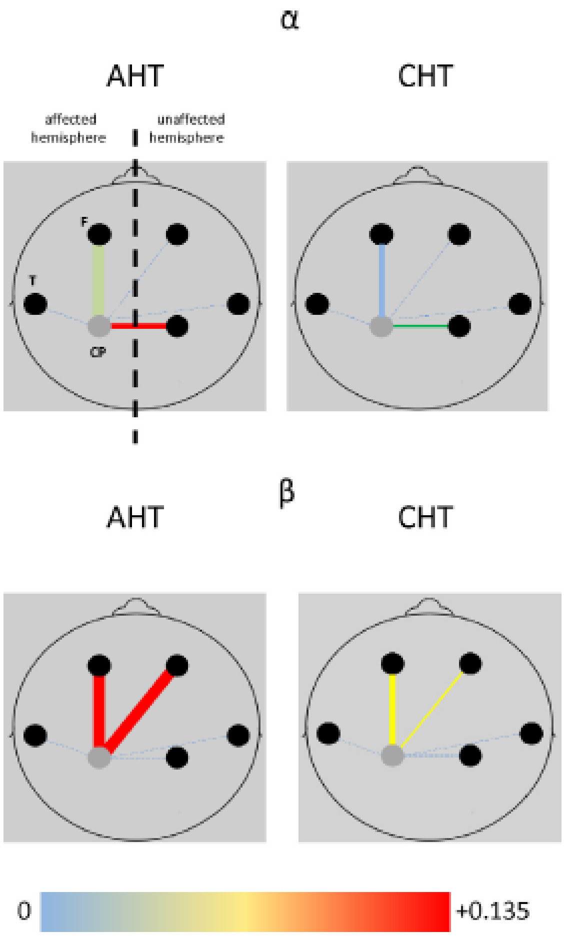
Objective: The objective of this study was the evaluation of the clinical and neurophysiological effects of intensive robot-assisted hand therapy compared to intensive occupational therapy in the chronic recovery phase after stroke.
Methods: 50 patients with a first-ever stroke occurred at least six months before, were enrolled and randomised into two groups. The experimental group was provided with the Amadeo™ hand training (AHT), whereas the control group underwent occupational therapist-guided conventional hand training (CHT). Both of the groups received 40 hand training sessions (robotic and conventional, respectively) of 45 min each, 5 times a week, for 8 consecutive weeks. All of the participants underwent a clinical and electrophysiological assessment (task-related coherence, TRCoh, and short-latency afferent inhibition, SAI) at baseline and after the completion of the training.
Results: The AHT group presented improvements in both of the primary outcomes (Fugl-Meyer Assessment for of Upper Extremity and the Nine-Hole Peg Test) greater than CHT (both $p < 0.001$). These results were paralleled by a larger increase in the frontoparietal TRCoh in the AHT than in the CHT group ($p < 0.001$) and a greater rebalance between the SAI of both the hemispheres ($p < 0.001$).
Conclusions: These data suggest a wider remodelling of sensorimotor plasticity and interhemispheric inhibition between sensorimotor cortices in the AHT compared to the CHT group.
Significance: These results provide neurophysiological support for the therapeutic impact of intensive robot-assisted treatment on hand function recovery in individuals with chronic stroke.

- Recovery depends on a large repertoire of functional and structural processes within the central nervous system, collectively termed neuroplasticity, which occur spontaneously or are induced by movement practise (Nudo, 2013).
- Intensive, repetitive, and task-oriented motor practises using neurorobotic devices assist recovery and rehabilitation (Krebs and Volpe, 2013; Pollock et al.,2014). In particular, the recovery of hand motor function after stroke has benefitted from the use of exoskeleton-based robots and end-effector systems, including the end-effectors robotic device AmadeoTM especially in the acute phase and in association with physiotherapy and/or occupational therapy (Sale et al., 2012, 2014).
- It has been suggested that robot-mediated training may potentially enhance neuroplasticity (Turner et al., 2013) by providing a haptic interaction and a consistent bulk of proprioceptive and/or other sensory inputs to motor outputs (Ramos-Murguialday et al., 2012).

There are significant changes in functional connectivity (coherence) within the fronto-parietal networks (inter- and intra-hemispheric functional connectivity) (Sergi et al., 2011) related to movement preparation and execution. Significant changes have been observed in both intra-cortical facilitation and inhibition and sensorimotor integration mechanisms of the primary motor cortices, assayed by Transcranial Magnetic Stimulation (TMS), related to actual motor status and functional outcome prediction, following ischaemic stroke (Alia et al., 2017; Seo et al., 2018).

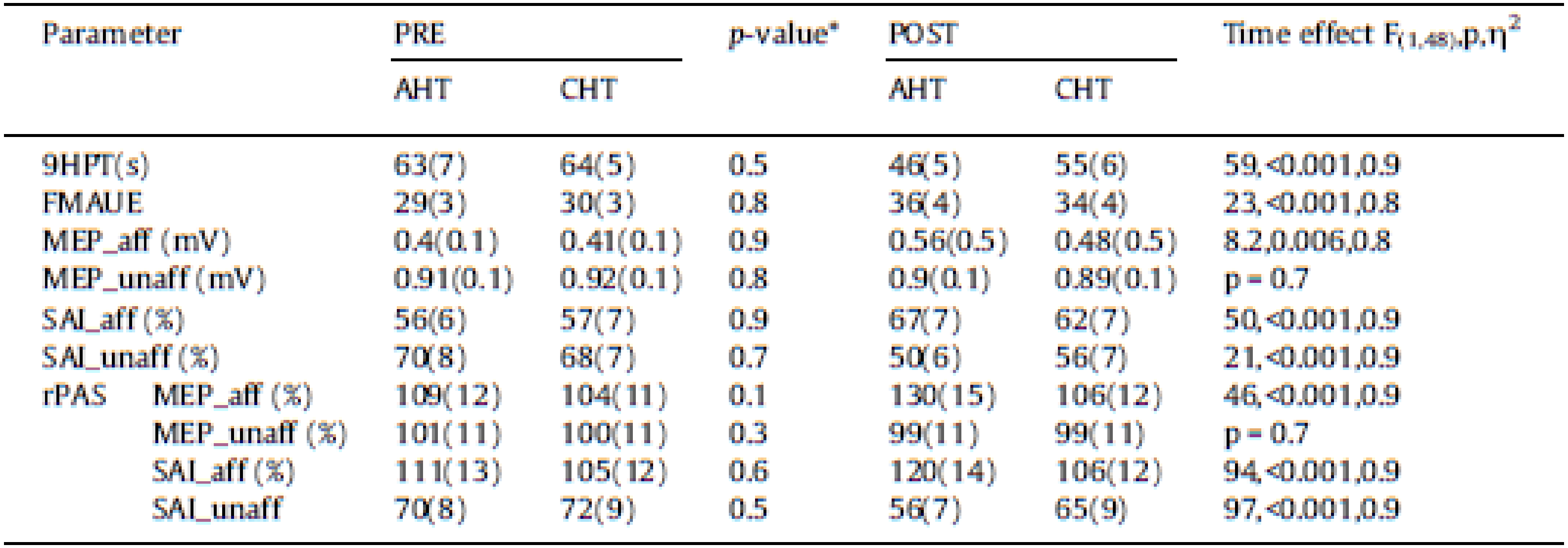
The patients in the AHT group underwent 40 individual conventional 3-hour physiotherapeutic training sessions, 5 days a week for 8 weeks (starting between 9:00 am and 11:00 am). The sessions were divided into 45 min of occupational therapy (daily living and reaching activities), 45 min of biomechanical training of both upper and lower limbs, 30 min of gait training, 30 min of speech therapy, and 30 min of rest period (distributed between the sessions) followed by 45 min of robot-assisted therapy of the affected limb using AmadeoTM.

The patients in the CHT group also underwent 40 individual conventional 3-hour physiotherapy sessions, followed by a 45 min conventional hand therapy session carried out by an occupational therapist, who both performed and assisted the patient in the execution of finger movements, reproducing the same experimental conditions of the AHT Group.



1- Both of the groups demonstrated a significant increase in alfa TRCoh between affected and unaffected CP ($p = 0.004$), while the AHT group had significantly higher Coh values compared to the CHT group (, $p < 0.001$). While AHT showed a considerable effect on Coh ($d = 0.9$; 0.57–1.19), the effect of CHT was moderate ($d = 0.3$; 0.19–0.41), with a consequent very large between-group difference.
A significant increase in beta TRCoh between affected CP and F was seen in both of the groups. The AHT group had significantly higher Coh values than the CHT group ($p = 0.002$).

2- Clinical improvement was paralleled by some electrophysiological changes. In particular, a more evident clinical improvement (estimated with the combined primary outcomes) was achieved when SAI in the affected hemisphere increased ($p < 0.001$), rPAS aftereffects in the unaffected hemisphere decreased ($p < 0.001$), and F–CP a TRCoh in the unaffected hemisphere increased ($p < 0.001$), which mainly involved the patients who practiced AHT. Moreover, the decrease in the rPAS after effects within the unaffected hemisphere, the increase in the rPAS after effects within the affected hemisphere, and the strengthening of F–CP b TRCoh within the unaffected hemisphere were significantly correlated ($p < 0.001$).



Parameter		PRE		p-value*	POST		Time effect $F_{(1,48)}$,p,η^2
		AHT	CHT		AHT	CHT	
9HPT(s)		63(7)	64(5)	0.5	46(5)	55(6)	59,<0.001,0.9
FMAUE		29(3)	30(3)	0.8	36(4)	34(4)	23,<0.001,0.8
MEP_aff (mV)		0.4(0.1)	0.41(0.1)	0.9	0.56(0.5)	0.48(0.5)	8.2,0.006,0.8
MEP_unaff (mV)		0.91(0.1)	0.92(0.1)	0.8	0.9(0.1)	0.89(0.1)	p = 0.7
SAI_aff (%)		56(6)	57(7)	0.9	67(7)	62(7)	50,<0.001,0.9
SAI_unaff (%)		70(8)	68(7)	0.7	50(6)	56(7)	21,<0.001,0.9
rPAS	MEP_aff (%)	109(12)	104(11)	0.1	130(15)	106(12)	46,<0.001,0.9
	MEP_unaff (%)	101(11)	100(11)	0.3	99(11)	99(11)	p = 0.7
	SAI_aff (%)	111(13)	105(12)	0.6	120(14)	106(12)	94,<0.001,0.9
	SAI_unaff	70(8)	72(9)	0.5	56(7)	65(9)	97,<0.001,0.9

DISCUSSION

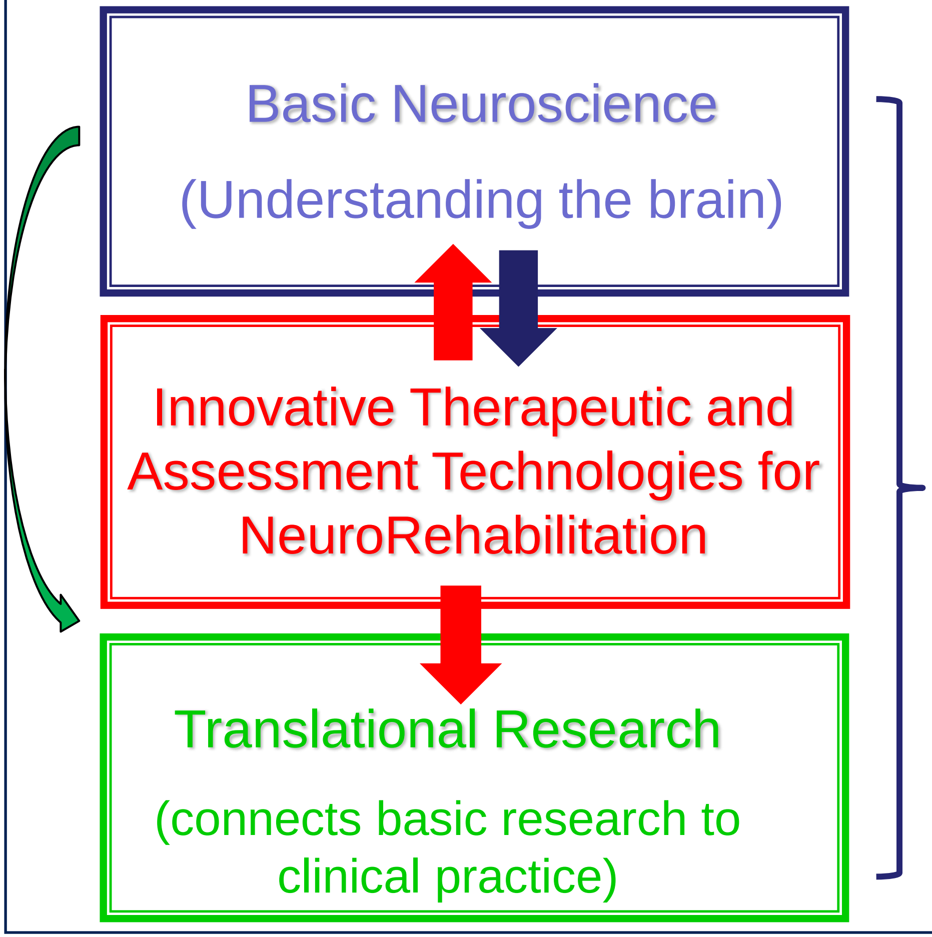
Specifically, restoring interhemispheric balance by reducing transcallosal inhibition, by providing the patients with intensive and repeatable robot–aided training exercises, is important for limiting use-dependent alterations in interhemispheric connectivity and preventing maladaptive plasticity (Takeuchi and Izumi, 2013), as well as removing the "plasticity brakes" exerted by perilesional or lesional tissues (Spalletti et al., 2017; Johansson, 2011).

The closely correlated changes in frontoparietal connectivity, sensorimotor integration, and interhemispheric plasticity provided by robotic rehabilitation may depend on a ''bottom–up" and/or a ''top–down" mechanism.

Traditional rehabilitation approaches, robotic technologies, and mechatronic devices can be qualified as "bottom–up" approaches, that is, they act at the bodily level (bottom) to influence the neural system (top), harnessing the mechanisms of neural plasticity (Krebs et al., 2009).
In addition they have been equipped with "enriched environments" to augment the generalising effect of spontaneous biological recovery instead of promoting compensation strategies (as in the case of AmadeoTM), for a "top–down" approach (Prieto et al., 2014; Chisari, 2015). Therefore, there could be a stronger fronto-parietal, "top–down" control from high–order to the primary sensorimotor areas.

Thus, it is possible to acquire some useful neurophysiological information on the plasticity-based recovery mechanisms after brain injury and following rehabilitation paradigm, so as to refine patient-tailored rehabilitative paradigm following stroke.

Integrazione tra robotica e neuroscienze



Basic Neuroscience

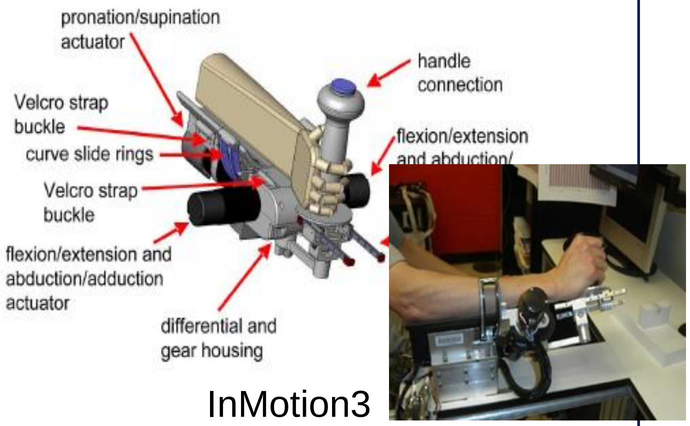
(Understanding the brain)

Innovative Therapeutic and Assessment Technologies for NeuroRehabilitation

Translational Research

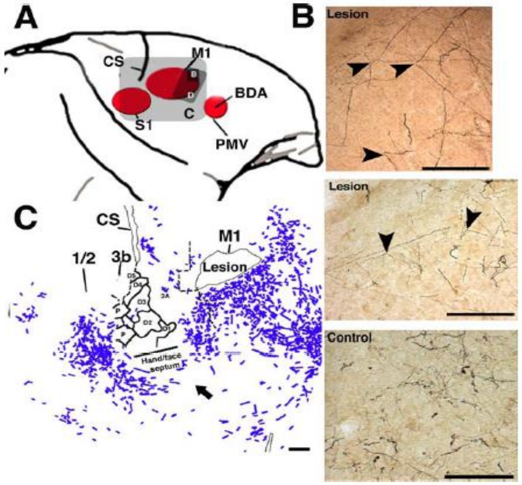
(connects basic research to clinical practice)

comprensione della neuroplasticità



InMotion3

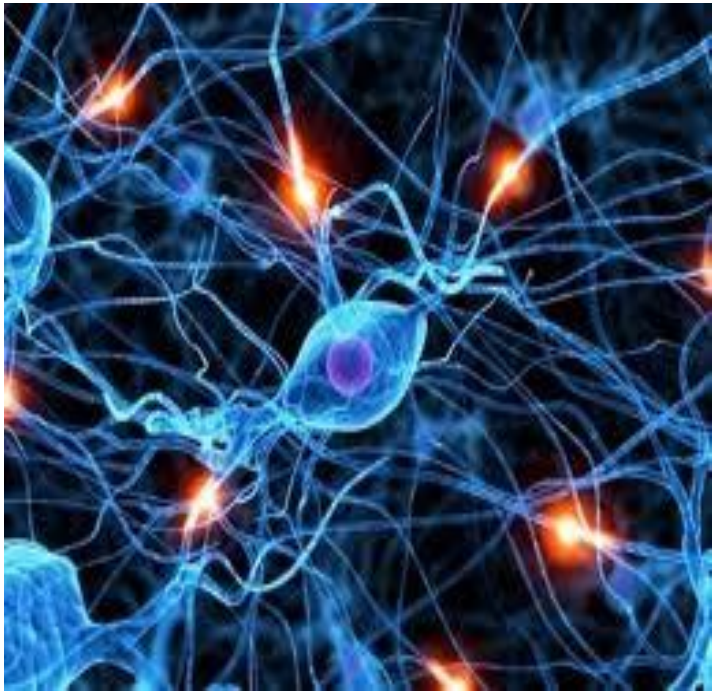
NEUROPLASTICITY is the key mechanism, object of neurorehabilitation intervention



Dancause et al. J Neurosci., 2005

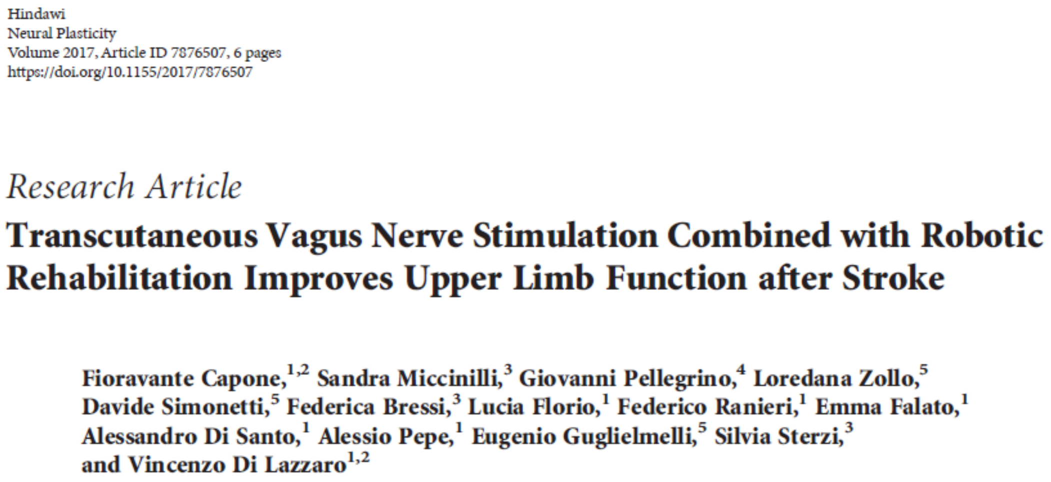
Neuroplasticità

Capacità del Sistema Nervoso di modificare la propria organizzazione funzionale a seguito di stimoli ambientali, alla pratica di compiti cognitivi e motori, in risposta ad agenti farmacologici e a lesioni del sistema nervoso centrale e periferico.



Si realizza mediante:

- Plasticità Sinaptica
- Fenomeni di «sprouting»
- Attivazione di aree potenzialmente in grado di assumere funzione vicaria
- Assunzione di funzioni suppletive da parte di strutture indenni



Hindawi
Neural Plasticity
Volume 2017, Article ID 7876507, 6 pages
https://doi.org/10.1155/2017/7876507

Research Article

Transcutaneous Vagus Nerve Stimulation Combined with Robotic Rehabilitation Improves Upper Limb Function after Stroke

**Fioravante Capone,[1,2] Sandra Miccinilli,[3] Giovanni Pellegrino,[4] Loredana Zollo,[5]
Davide Simonetti,[5] Federica Bressi,[3] Lucia Florio,[1] Federico Ranieri,[1] Emma Falato,[1]
Alessandro Di Santo,[1] Alessio Pepe,[1] Eugenio Guglielmelli,[5] Silvia Sterzi,[3]
and Vincenzo Di Lazzaro[1,2]**

The efficacy of standard rehabilitative therapy for improving upper limb functions after stroke is limited; thus, alternative strategies are needed. Vagus nerve stimulation (VNS) paired with rehabilitation is a promising approach, but the invasiveness of this technique limits its clinical application. Recently, a noninvasive method to stimulate vagus nerve has been developed.

The aim of the present study was to explore whether noninvasive VNS combined with robotic rehabilitation can enhance upper limb Functionality in chronic stroke.
Fourteen patients with either ischemic or haemorrhagic chronic stroke were randomized to robot-assisted therapy associated with real or sham VNS, delivered for 10 working days. Efficacy was evaluated by change in upper extremity Fugl–Meyer score. After intervention, there were no adverse events and Fugl–Meyer scores were significantly better in the real group compared to the sham group.

Compared to traditional stimulation, noninvasive VNS seems to be safer and more tolerable.
Further studies are needed to confirm the efficacy of this innovative approach.

- ✓ *Several studies have explored the possibility to potentiate the effect of robotic therapy by the association with noninvasive human brain stimulation techniques, such as repetitive transcranial magnetic stimulation (rTMS), that can induce neuroplasticity via long-term potentiation-/depression- (LTP-/LTD-) like phenomenA.*

……

- ✓ *The literature analysis of the published data seems to demonstrate that the association of rTMS with robotic training has the same clinical gain derived from robotic therapy alone.*
- ✓ *rTMS is contraindicated in patients who suffered from haemorrhagic stroke for the risk of inducing seizures.*

Vagus nerve stimulation (VNS) is approved as adjunctive treatment for refractory epilepsy and depression.

Recent studies have demonstrated that VNS paired with rehabilitation significantly improves forelimb strength and movement speed in rat models of ischemic and haemorrhagic stroke.

VNS is believed to enhance the benefits of rehabilitation by promoting neuroplasticity.

The aim of the present study was to explore whether tVNS can enhance the benefit induced by robotic rehabilitation on motor function of the upper limb in chronic stroke.

MATERIALI E METODI

Seven patients were randomized to robot-assisted therapy associated with real tVNS and seven patients to robot assisted therapy associated with sham tVNS.

A total of 12 patients completed the study: 7 real (mean age: 53.7± 15.6 years, 4 males) and 5 sham (mean age: 55.6 ± 15.9 years, 3 males). The real and sham groups were not significantly different regarding age, sex, type of stroke (haemorrhagic versus ischemic), and side of lesion.
Time elapsed from stroke onset and clinical status at baseline (in particular, FMA score) were different between the two groups, but this difference was not statistically significant (*p* > 0 200 consistently) .

After intervention, FMA scores were significantly better in the real group as compared to the sham group (Mann– Whitney U = 5 00, p = 0 048) .

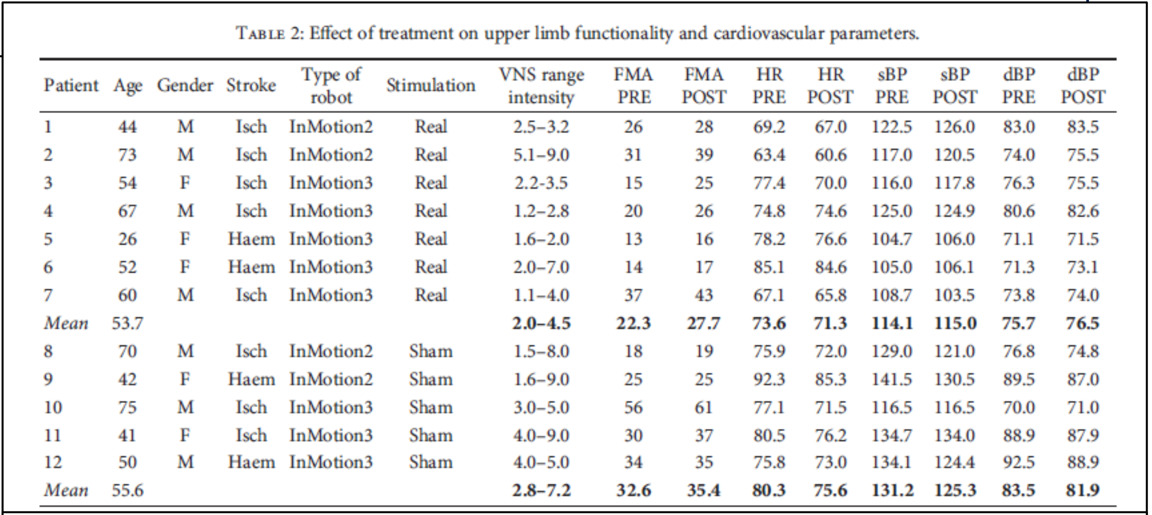
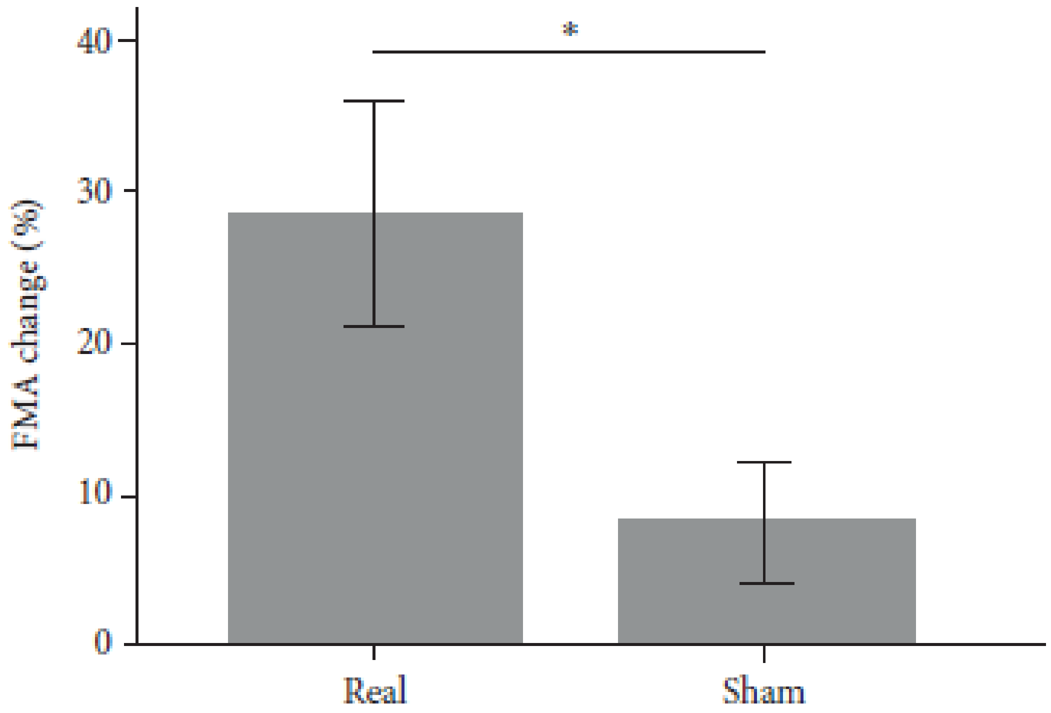


Table 2: Effect of treatment on upper limb functionality and cardiovascular parameters.

Patient	Age	Gender	Stroke	Type of robot	Stimulation	VNS range intensity	FMA PRE	FMA POST	HR PRE	HR POST	sBP PRE	sBP POST	dBP PRE	dBP POST
1	44	M	Isch	InMotion2	Real	2.5–3.2	26	28	69.2	67.0	122.5	126.0	83.0	83.5
2	73	M	Isch	InMotion2	Real	5.1–9.0	31	39	63.4	60.6	117.0	120.5	74.0	75.5
3	54	F	Isch	InMotion3	Real	2.2-3.5	15	25	77.4	70.0	116.0	117.8	76.3	75.5
4	67	M	Isch	InMotion3	Real	1.2–2.8	20	26	74.8	74.6	125.0	124.9	80.6	82.6
5	26	F	Haem	InMotion3	Real	1.6–2.0	13	16	78.2	76.6	104.7	106.0	71.1	71.5
6	52	F	Haem	InMotion3	Real	2.0–7.0	14	17	85.1	84.6	105.0	106.1	71.3	73.1
7	60	M	Isch	InMotion3	Real	1.1–4.0	37	43	67.1	65.8	108.7	103.5	73.8	74.0
Mean	53.7					**2.0–4.5**	**22.3**	**27.7**	**73.6**	**71.3**	**114.1**	**115.0**	**75.7**	**76.5**
8	70	M	Isch	InMotion2	Sham	1.5–8.0	18	19	75.9	72.0	129.0	121.0	76.8	74.8
9	42	F	Haem	InMotion2	Sham	1.6–9.0	25	25	92.3	85.3	141.5	130.5	89.5	87.0
10	75	M	Isch	InMotion3	Sham	3.0–5.0	56	61	77.1	71.5	116.5	116.5	70.0	71.0
11	41	F	Isch	InMotion3	Sham	4.0–9.0	30	37	80.5	76.2	134.7	134.0	88.9	87.9
12	50	M	Haem	InMotion3	Sham	4.0–5.0	34	35	75.8	73.0	134.1	124.4	92.5	88.9
Mean	55.6					**2.8–7.2**	**32.6**	**35.4**	**80.3**	**75.6**	**131.2**	**125.3**	**83.5**	**81.9**



CONCLUSIONS

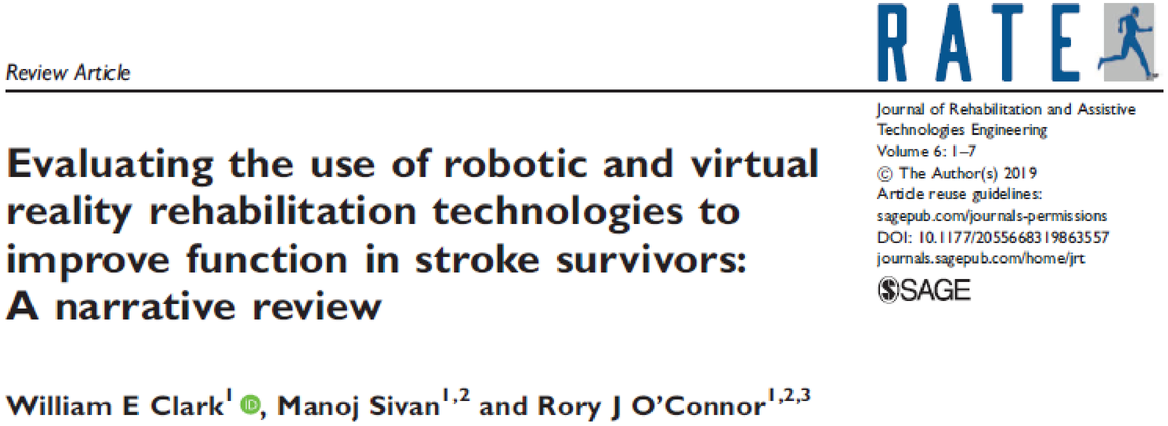
This is the first study that has evaluated the feasibility of tVNS in chronic both ischemic and haemorrhagic stroke.

A potential benefit of invasive VNS in chronic stroke has been recently described both in animal model and in patients. In a rat model of chronic stroke, Khodaparast et al. have demonstrated that VNS paired with rehabilitative training significantly improves recovery of forelimb function compared to rehabilitation alone.

According to the authors, this finding suggests that, in chronic stroke, VNS promotes recovery through a mechanism independent of neuroprotection, most likely by inducing neuroplasticity. VNS increases levels of brain-derived neurotrophic factor (BDNF) and neurotransmitters such as noradrenaline linked to neuroplasticity and recovery after brain lesion.

As described for rTMS, tVNS could increase the effect of rehabilitation by producing a priming effect on subsequent motor training.

The present study has some important limitations such as the small sample size, the use of different kind of robotic training, and the lack of a long-term follow-up.



Review Article

RATE
Journal of Rehabilitation and Assistive Technologies Engineering
Volume 6: 1–7
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SAGE

Evaluating the use of robotic and virtual reality rehabilitation technologies to improve function in stroke survivors: A narrative review

William E Clark[1], **Manoj Sivan**[1,2] **and Rory J O'Connor**[1,2,3]

This review evaluates the effectiveness of robotic and virtual reality technologies used for neurological rehabilitation in stroke survivors. It examines each rehabilitation technology in turn before considering combinations of these technologies and the complexities of rehabilitation outcome assessment. There is high-quality evidence that upper-limb robotic rehabilitation technologies improve movement, strength and activities of daily living, whilst the evidence for robotic lower-limb rehabilitation is currently not as convincing. Virtual reality technologies also improve activities of daily living.

Whilst the benefit of these technologies over dose-controlled conventional rehabilitation is likely to be small, there is a role for both technologies as part of a broader rehabilitation programme, where they may help to increase the intensity and amount of therapy delivered.
Combining robotic and virtual reality technologies in a rehabilitation programme may further improve rehabilitation outcomes and we would advocate randomised controlled trials of these technologies in combination.

ROBOT

One of the major limitations of conventional rehabilitation programmes is an inadequate dose of rehabilitation therapy, in terms of repetition and intensity.

The current evidence suggests that there is a high practice threshold required to achieve significant upper-limb functional improvements. This threshold is achievable in humans to deliver the repetition and intensity that are thought to be important in experience-dependent plasticity.

Rehabilitation technology development has been identified as a priority area for research by the Medical Rehabilitation Research Coordinating committee (USA).

Upper-limb robotics improve ADLs at least as much as conventional therapy, but there is currently insufficient evidence of superiority.

The greatest benefits in independence in walking and walking speed were achieved by participants who were non-ambulatory at the start of the study and in those for whom the interventions were applied early post-stroke.

VR

1. VR can be used for simulated independent practice at higher doses than that could be achieved through conventional therapy. These technologies therefore share some of the benefits of robotics in terms of increasing training intensity and repetitions, and reducing therapist time. The typical portrayal in the lay media of VR is usually that of a so-called ‘immersive’ VR, with a head-mounted screen. Commercially available video gaming systems have been adapted for use in VR rehabilitation.

2. It is recognised that feedback plays an important role in skill acquisition and is an essential element in experience-dependent plasticity. In motor learning, it is important to receive feedback not just on the end results – ‘success or failure’ – but on movement performance; this is possible with the use of VR technologies.

3. There is growing interest in VR technologies, the most up-to-date Cochrane review found a significant benefit to upper-limb function with a moderate effect size when VR was used as an adjunct to usual care but not when compared to dose-controlled conventional therapy.

- In summary, there is high-quality evidence that upper-limb robotic technology is as effective as dose-controlled conventional therapy at improving ADLs, motor function and strength.

- There is a small benefit in ADLs with VR technologies as compared to dose-controlled conventional therapy.

- Both technologies can be beneficial as part of a broader rehabilitation programme and may help to improve the intensity and amount of rehabilitation delivered.

- There is a need for RCTs of combined VR and robotic technologies. They should assess a range of outcomes corresponding to the ICF framework and include measures of ADL, cognition, QOL and costeffectiveness.

CONSENSUS

Quali sono gli effetti della terapia robotica per l’arto superiore nel paziente con ictus cerebrale?

ICF

distinti per esoscheletri, End-Effector e dispositivi per la mano

nel paziente con ictus acuto-subacuto?

nel paziente con ictus cronico?

nei pazienti affetti da altre lesioni del sistema nervoso centrale: lesione del midollo spinale, sclerosi multipla, grave cerebrolesione acquisita e malattia di Parkinson?

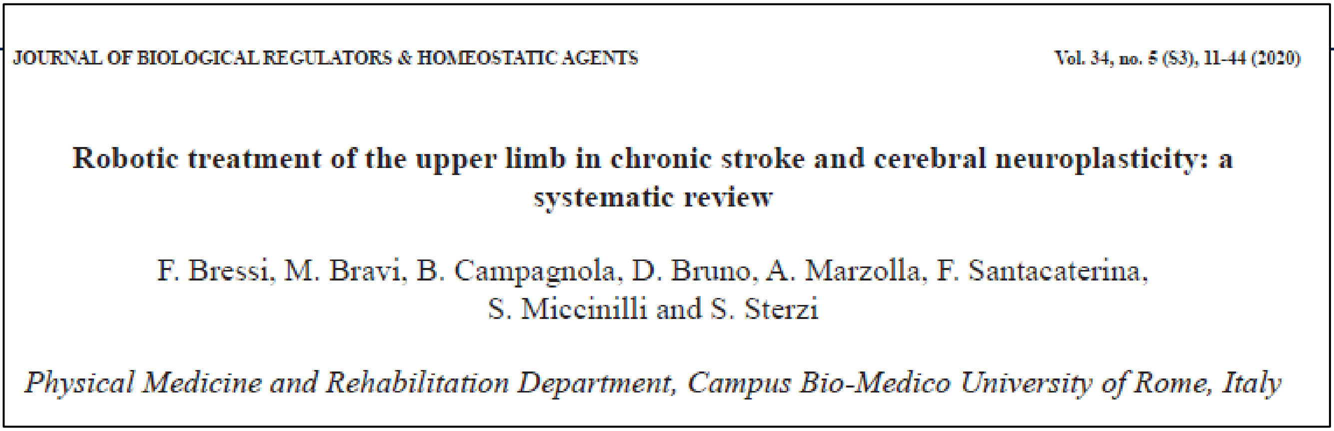
QUALI DUBBI…….

La valutazione di efficacia dei robot per l’arto superiore è resa difficile dalla particolare complessità dell’arto superiore, che implica la funzione dell’esplorazione a maggiore coinvolgimento della spalla e del gomito e della funzione della presa a maggiore coinvolgimento della mano. Esistono inoltre compiti funzionali bimanuali con specifiche possibilità riabilitative.

L’importante diffusione dei robot nella riabilitazione non è accompagnata da un altrettanto accordo sull’efficacia (Rodgers et al 2019, Mehrolz et al 2018) ed in particolare su quali siano i pazienti che possano beneficiare maggiormente in termini di gravità, distanza dall’evento acuto e con quale o quali tipi di robot.

Altro punto importante ove non vi è accordo e che necessita di valutazione per una migliore pratica clinica è l’endpoint della raccomandabilità: probabilmente una migliore definizione di questo aspetto genererebbe una migliore integrazione della terapia assistita da robot al progetto riabilitativo individuale.

Mancano quasi del tutto, infine, indicazioni sulla dose e frequenza di somministrazione dei protocolli di rieducazione mediante dispositivi robotici. Tali indicazioni sono necessarie ai clinici per implementare il processo decisionale terapeutico e per meglio definire il campo di applicazione e le modalità della tecnologia robotica nell’ambito della neuro-riabilitazione dell’arto superiore.



JOURNAL OF BIOLOGICAL REGULATORS & HOMEOSTATIC AGENTS Vol. 34, no. 5 (S3), 11-44 (2020)

Robotic treatment of the upper limb in chronic stroke and cerebral neuroplasticity: a systematic review

F. Bressi, M. Bravi, B. Campagnola, D. Bruno, A. Marzolla, F. Santacaterina,
S. Miccinilli and S. Sterzi

Physical Medicine and Rehabilitation Department, Campus Bio-Medico University of Rome, Italy

This systematic review was conducted using PubMed, PEDro, Cinahl (EBSCOhost), Scopus and Cochrane databases. The research was carried out until February 2020 it included articles written in English language, published between 2009 and 2020, and the outcomes considered were neuroplasticity assessments.

We included 23 studies over 6145 records identified from the preliminary research. The selected studies proposed different methods for neuroplasticity assessment (i.e. transcranial direct current stimulation (tDCS), EEG-Based Brain Computer Interface (BCI) and Neuroimaging (fMRI)), and different Robotic Rehabilitation treatments. These studies demonstrated a positive correlation between changes in central nervous circuits and post-treatment clinical outcomes.

Our study has highlighted the effectiveness of robotic therapy in promoting mechanisms that facilitate re-learning and motor recovery in patients with post-stroke chronic disabilities.

Future studies should overcome the limitations in the current literature, by proposing:

- **a greater number of high-level RCTs**
- **-understand the mechanisms of robot-induced neuroplasticity**
- **estimate a prognosis of recovery of motor function**
- **plan a personalized rehabilitative programme**

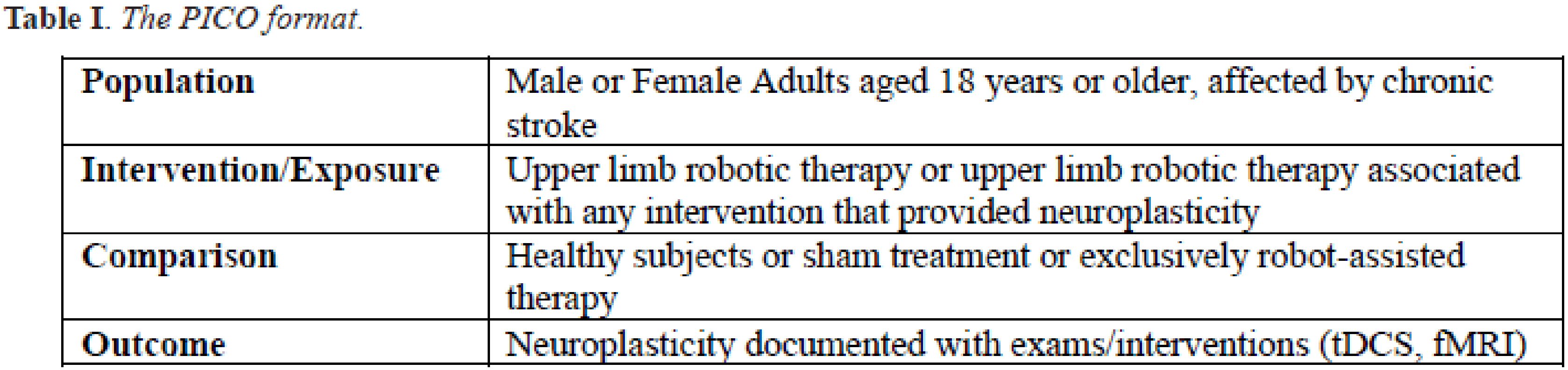


Table I. *The PICO format.*

Population	Male or Female Adults aged 18 years or older, affected by chronic stroke
Intervention/Exposure	Upper limb robotic therapy or upper limb robotic therapy associated with any intervention that provided neuroplasticity
Comparison	Healthy subjects or sham treatment or exclusively robot-assisted therapy
Outcome	Neuroplasticity documented with exams/interventions (tDCS, fMRI)

TERAPIA A DOMICILIO

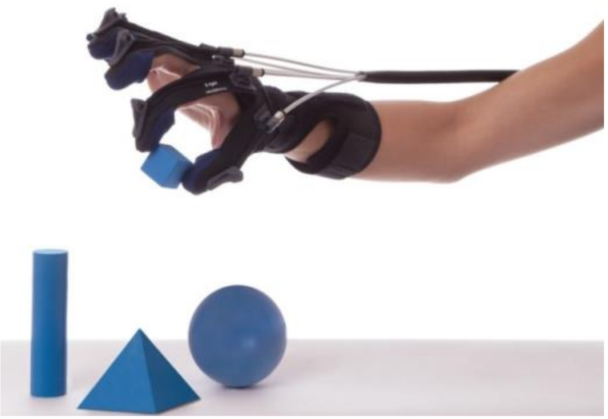
GLOREHA SINFONIA

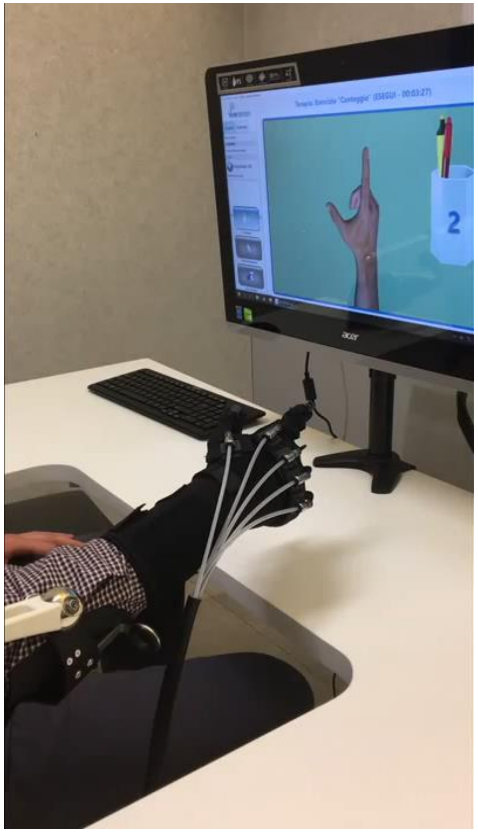
- Dispositivo a supporto della riabilitazione dell’arto superiore, accompagna il paziente in tutte le fasi del recupero neuromotorio.

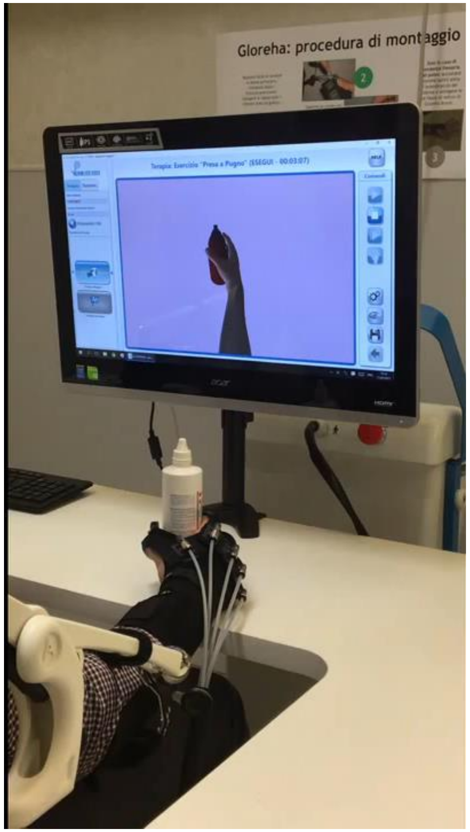
- E’ in grado di supportare il movimento delle articolazioni delle dita e riconoscere i movimenti attivi prodotti spontaneamente dal paziente.

- Una stimolazione multisensoriale accompagna gli esercizi motori e coinvolge il paziente grazie all’animazione 3D della mano sullo schermo.

- A seconda delle esigenze del trattamento, il movimento può essere prodotto interamente dal guanto robotico o interamente dal pz oppure il dispositivo interviene a supporto dello sforzo motorio del paziente.







Il **DISPOSITIVO** comprende :

- PC TOUCHSCREEN CON SOFTWARE INTERATTIVO
- «TENDINI ARTIFICIALI» PER LA MOBILIZZAZIONE PASSIVA, ATTIVA E ATTIVO-ASSISTITA
- SENSORI PER LA LETTURA DEI MOVIMENTI ATTIVI
- SUPPORTO DINAMICO DEL BRACCIO
- POSSIBILITA' DI UN BILATERAL TRAINING

GLOREHA SINFONIA

Il Guanto Robotico permette:

1) *Esercizi Funzionali task-oriented*: riapprendimento delle capacità di esecuzione di azioni di vita quotidiana attraverso esercizi di grasping, reaching, picking con oggetti reali.

2) *Compensazione di carico:* due supporti dinamici sgravano il peso dell’arto superiore e favoriscono l’esecuzione di esercizi funzionali.

3) *Action-Observation Therapy*: propone per ogni esercizio la possibilità di uno svolgimento in due tempi, osservazione ed esecuzione.

4) *Bilateral Training*: «sfrutta» il movimento della mano sana per generare, tramite il guanto robotico, un movimento similare sulla mano affetta.

5) *Raddoppiamento delle potenzialità riabilitative:* meccanismo motorio a specchio, osservazione delle due mani in 3D, esecuzione di task funzionali bilaterali con oggetti reali.

GLOREHA SINFONIA

MONITORAGGIO DELLE PERFORMANCE, PASSO DOPO PASSO

Il Guanto Robotico registra tutti i dati associati a ciascun paziente e consente al professionista clinico di tenere monitorato l’andamento delle performance di ogni soggetto trattato.

Grafici intuitivi mostrano il trend dei risultati conseguiti, esercizio per esercizio, sessione dopo sessione.

Il pz può avere un feed-back diretto sui progressi conseguiti.

GLOREHA SINFONIA

BENEFICI CLINICI

1. MANTENIMENTO E MIGLIORAMENTO DEL RANGE ARTICOLARE
2. PREVENZIONE DI ADERENZE, CONTRATTURE, DANNI DA IMMOBILIZZAZIONE
3. RIDUZIONE DEL DOLORE, DELL’EDEMA E DELL’IPERTONO
4. STIMOLAZIONE PROPRIOCETTIVA
5. MIGLIORAMENTO DEL METABOLISMO ARTICOLARE E DELLA CIRCOLAZIONE LINFATICA E SANGUIGNA

GLOREHA SINFONIA

BENEFICI CLINICI (2)

6. MANTENIMENTO DELLE AFFERENZE FUNZIONALI E DELLA PERCEZIONE DEL PROPRIO CORPO

7. INCREMENTO DELLA COORDINAZIONE, DELLA DESTREZZA E DELL'INDIPENDENZA FUNZIONALE

8. AUMENTO DELLA FORZA DI PRESA E DI PINZA

9. MIGLIORAMENTO DELLE CAPACITA' VISUO-SPAZIALI E ATTENTIVE

GLOREHA SINFONIA

- “Effects of contralesional robot-assisted hand training in patients with **unilateral spatial neglect** following stroke: a case series study”; Valentina Varalta et al., Journal of NeuroEngineering and Rehabilitation 2014

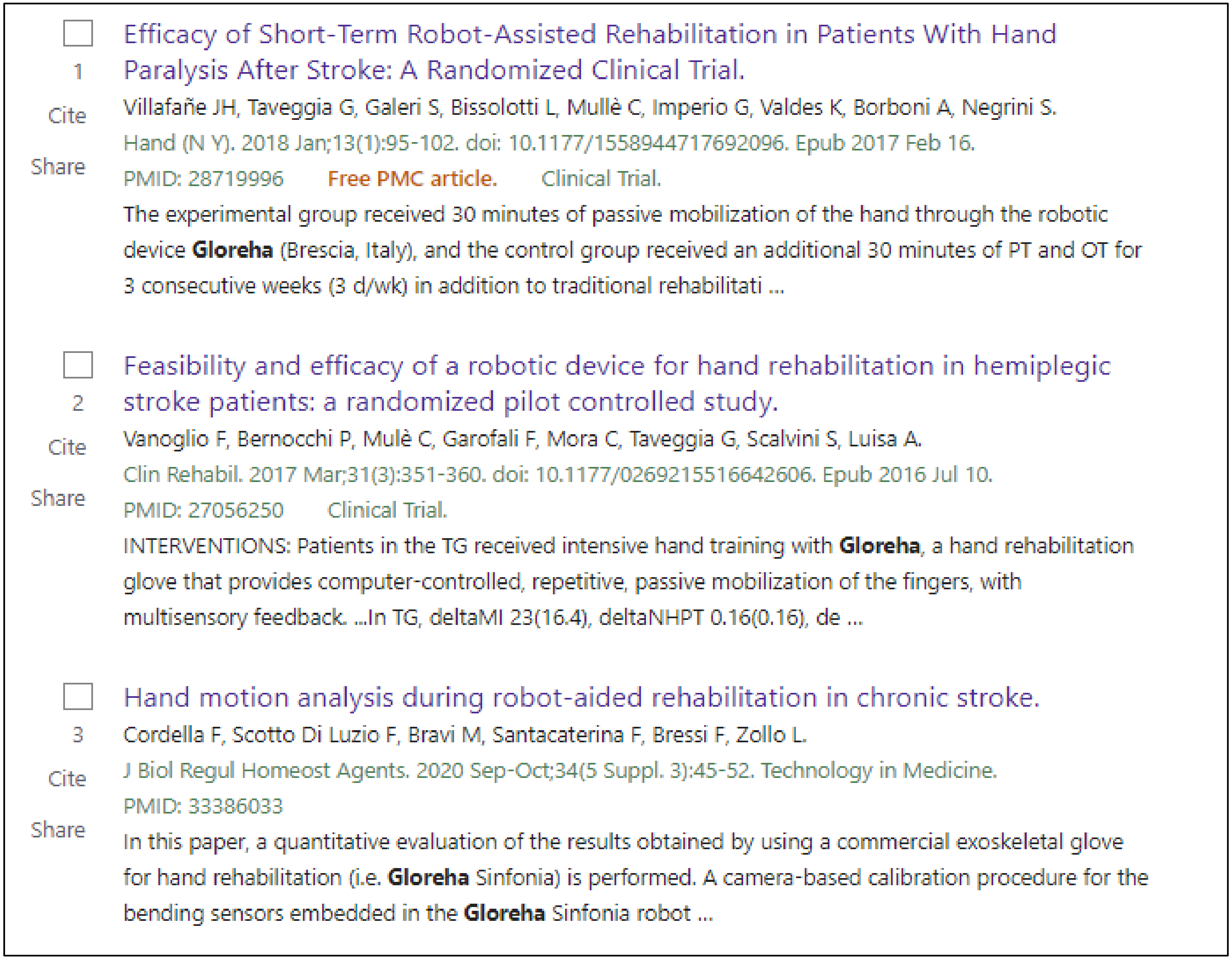
- “Feasibility and efficacy of a robotic device for hand rehabilitation in hemiplegic stroke patients: a **randomized pilot controlled study**”; Fabio Vanoglio et al., Clin Rehabil. 2016 Apr 7

- “**Changes in skeletal muscle perfusion and spasticity** in patient with poststroke hemiparesis treated by robotic assistance (Gloreha) of the hand”; Luciano Bissolotti et al., J. Phys. Ther. Sci. 2016

- “Is passive mobilization robot-assisted therapy effective in upper limb motor recovery in patient with acquired Brain Injury? A **randomized crossover trial**”; Maria Giulia Montecchi et al., Int J Phys Ther Rehab 2016

- “Robotic Glove with virtual reality biofeedback in spasticity management on **acute and chronic patients** with spastic hand paresis: impact on goal oriented functional therapy and routine mass therapy”; Jakub Pětioký et al., presented at the 20th ESPRM Congress (2016)

GLOREHA SINFONIA



☐ 1

Cite

Share

Efficacy of Short-Term Robot-Assisted Rehabilitation in Patients With Hand Paralysis After Stroke: A Randomized Clinical Trial.

Villafañe JH, Taveggia G, Galeri S, Bissolotti L, Mullè C, Imperio G, Valdes K, Borboni A, Negrini S.

Hand (N Y). 2018 Jan;13(1):95-102. doi: 10.1177/1558944717692096. Epub 2017 Feb 16.

PMID: 28719996 Free PMC article. Clinical Trial.

The experimental group received 30 minutes of passive mobilization of the hand through the robotic device **Gloreha** (Brescia, Italy), and the control group received an additional 30 minutes of PT and OT for 3 consecutive weeks (3 d/wk) in addition to traditional rehabilitati ...

☐ 2

Cite

Share

Feasibility and efficacy of a robotic device for hand rehabilitation in hemiplegic stroke patients: a randomized pilot controlled study.

Vanoglio F, Bernocchi P, Mulè C, Garofali F, Mora C, Taveggia G, Scalvini S, Luisa A.

Clin Rehabil. 2017 Mar;31(3):351-360. doi: 10.1177/0269215516642606. Epub 2016 Jul 10.

PMID: 27056250 Clinical Trial.

INTERVENTIONS: Patients in the TG received intensive hand training with **Gloreha**, a hand rehabilitation glove that provides computer-controlled, repetitive, passive mobilization of the fingers, with multisensory feedback. ...In TG, deltaMI 23(16.4), deltaNHPT 0.16(0.16), de ...

☐ 3

Cite

Share

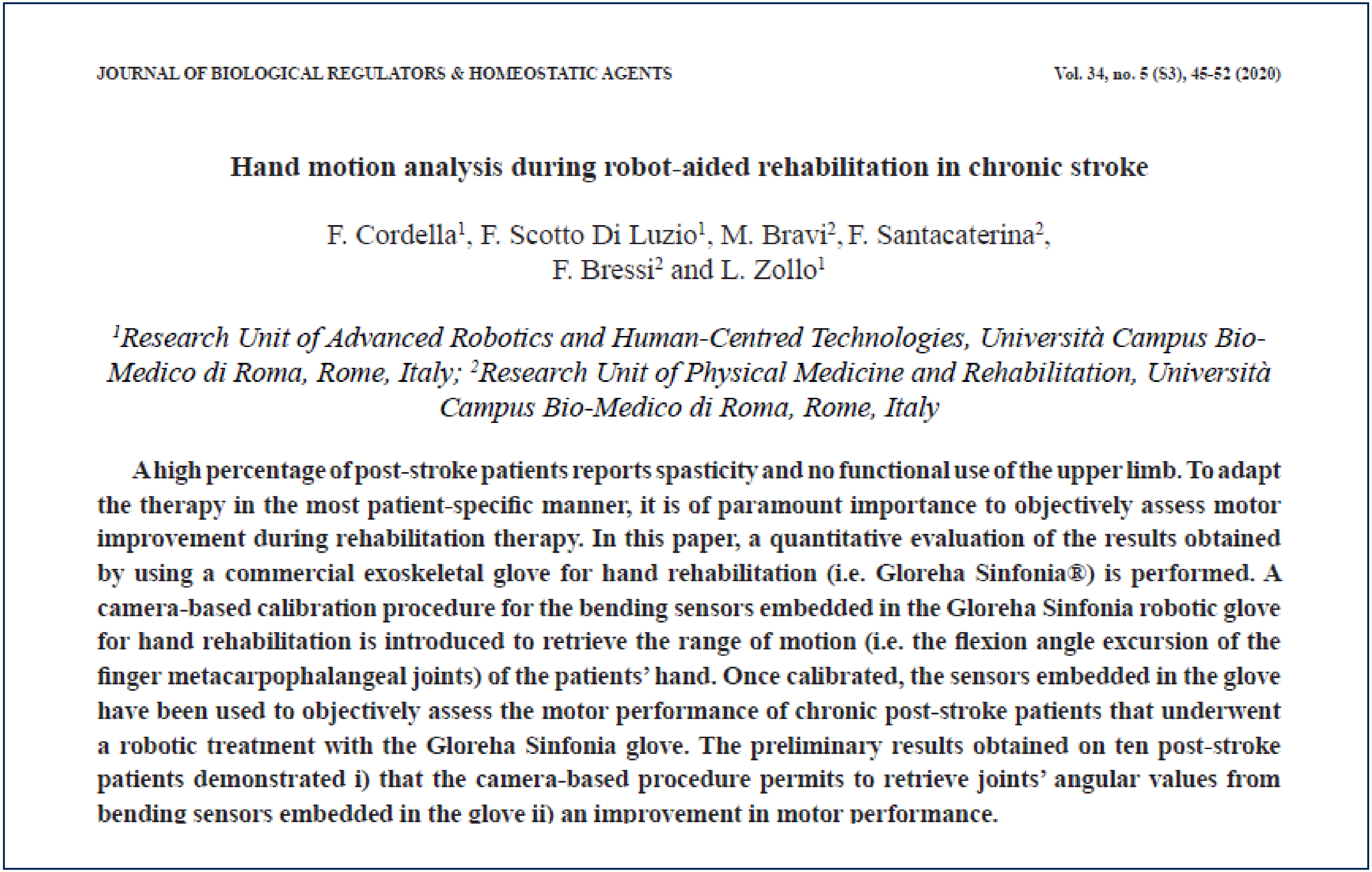
Hand motion analysis during robot-aided rehabilitation in chronic stroke.

Cordella F, Scotto Di Luzio F, Bravi M, Santacaterina F, Bressi F, Zollo L.

J Biol Regul Homeost Agents. 2020 Sep-Oct;34(5 Suppl. 3):45-52. Technology in Medicine.

PMID: 33386033

In this paper, a quantitative evaluation of the results obtained by using a commercial exoskeletal glove for hand rehabilitation (i.e. **Gloreha** Sinfonia) is performed. A camera-based calibration procedure for the bending sensors embedded in the **Gloreha** Sinfonia robot ...



JOURNAL OF BIOLOGICAL REGULATORS & HOMEOSTATIC AGENTS Vol. 34, no. 5 (S3), 45-52 (2020)

Hand motion analysis during robot-aided rehabilitation in chronic stroke

F. Cordella[1], F. Scotto Di Luzio[1], M. Bravi[2], F. Santacaterina[2],
F. Bressi[2] and L. Zollo[1]

[1]Research Unit of Advanced Robotics and Human-Centred Technologies, Università Campus Bio-Medico di Roma, Rome, Italy; [2]Research Unit of Physical Medicine and Rehabilitation, Università Campus Bio-Medico di Roma, Rome, Italy

A high percentage of post-stroke patients reports spasticity and no functional use of the upper limb. To adapt the therapy in the most patient-specific manner, it is of paramount importance to objectively assess motor improvement during rehabilitation therapy. In this paper, a quantitative evaluation of the results obtained by using a commercial exoskeletal glove for hand rehabilitation (i.e. Gloreha Sinfonia®) is performed. A camera-based calibration procedure for the bending sensors embedded in the Gloreha Sinfonia robotic glove for hand rehabilitation is introduced to retrieve the range of motion (i.e. the flexion angle excursion of the finger metacarpophalangeal joints) of the patients' hand. Once calibrated, the sensors embedded in the glove have been used to objectively assess the motor performance of chronic post-stroke patients that underwent a robotic treatment with the Gloreha Sinfonia glove. The preliminary results obtained on ten post-stroke patients demonstrated i) that the camera-based procedure permits to retrieve joints' angular values from bending sensors embedded in the glove ii) an improvement in motor performance.

Fig. 2. *Experimental Setup for the Gloreha Sinfonia glove calibration.*

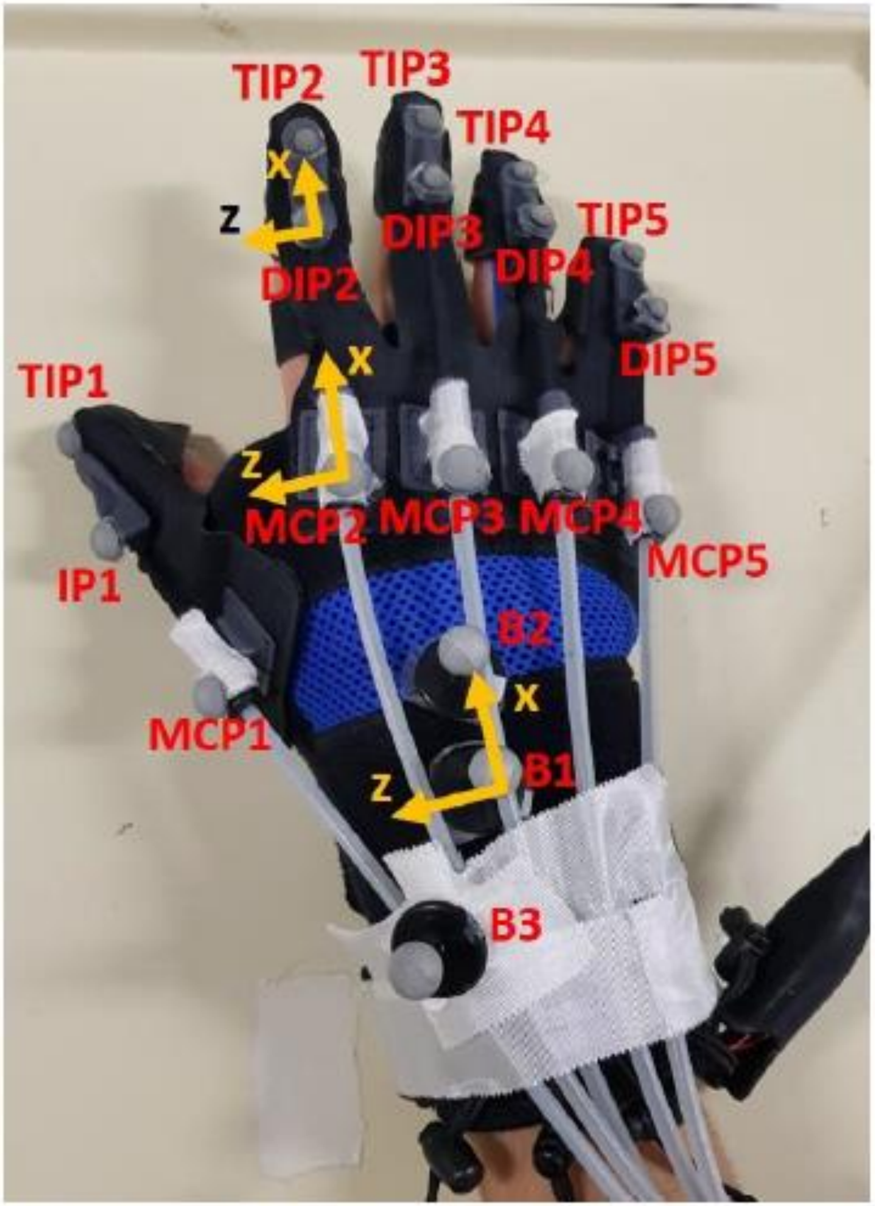


Fig. 3. *Protocol for marker placement. Marker names are outlined in red and the reference frames are shown in yellow.*

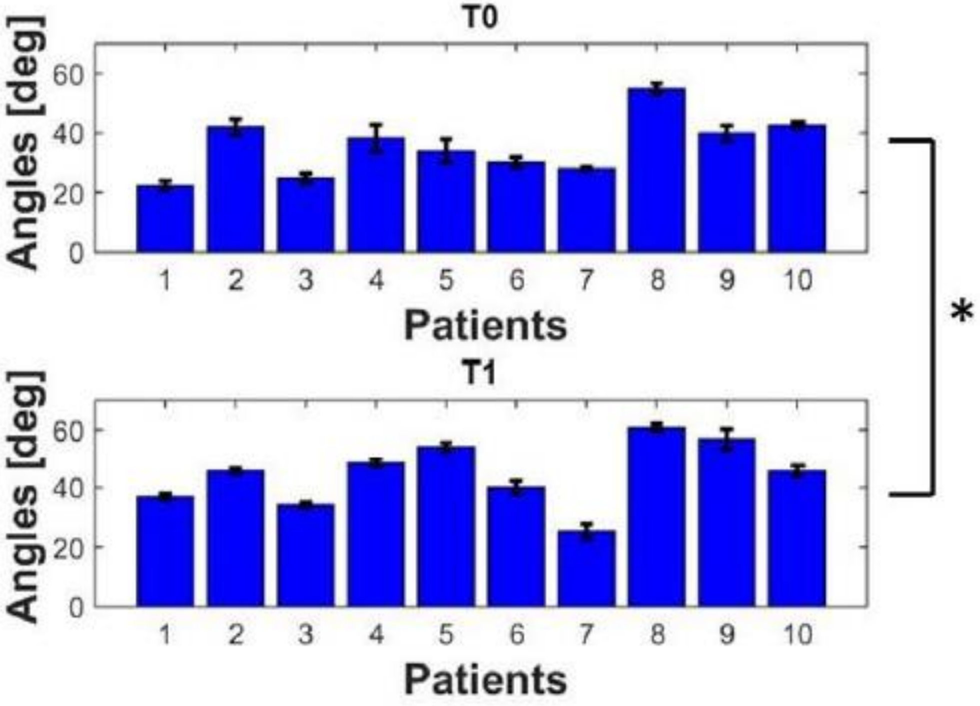


Fig. 4. *Mean value and standard deviation of the ROM of all the fingers measured for each patient at T 0 (up) and T 1 (bottom). Statistical significance between ROM computed at T0 and at T1 is indicated with *.*

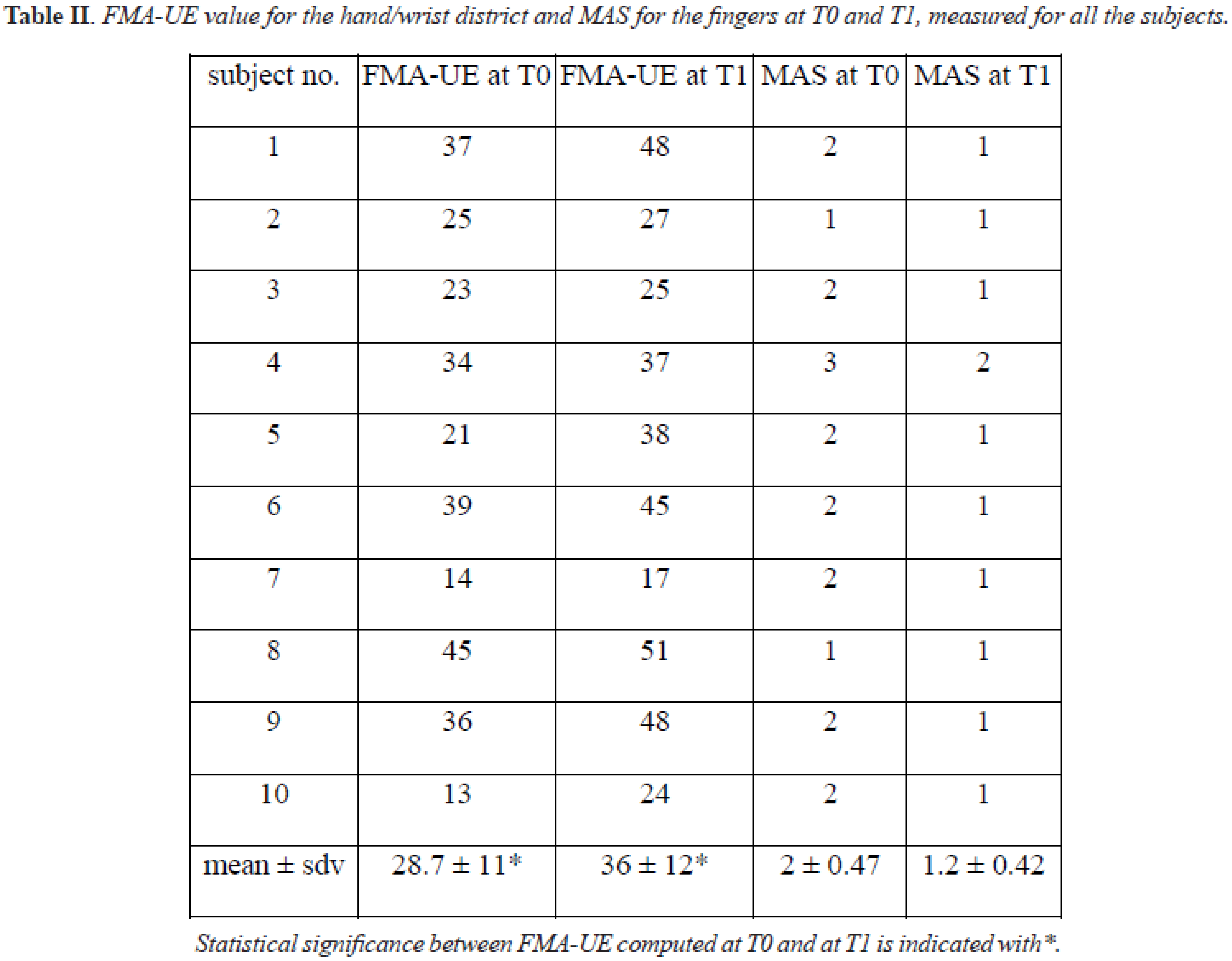


Table II. *FMA-UE value for the hand/wrist district and MAS for the fingers at T0 and T1, measured for all the subjects.*

subject no.	FMA-UE at T0	FMA-UE at T1	MAS at T0	MAS at T1
1	37	48	2	1
2	25	27	1	1
3	23	25	2	1
4	34	37	3	2
5	21	38	2	1
6	39	45	2	1
7	14	17	2	1
8	45	51	1	1
9	36	48	2	1
10	13	24	2	1
mean ± sdv	28.7 ± 11*	36 ± 12*	2 ± 0.47	1.2 ± 0.42

Statistical significance between FMA-UE computed at T0 and at T1 is indicated with.*

frontiers in
SYSTEMS NEUROSCIENCE

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Augmentation-related brain plasticity

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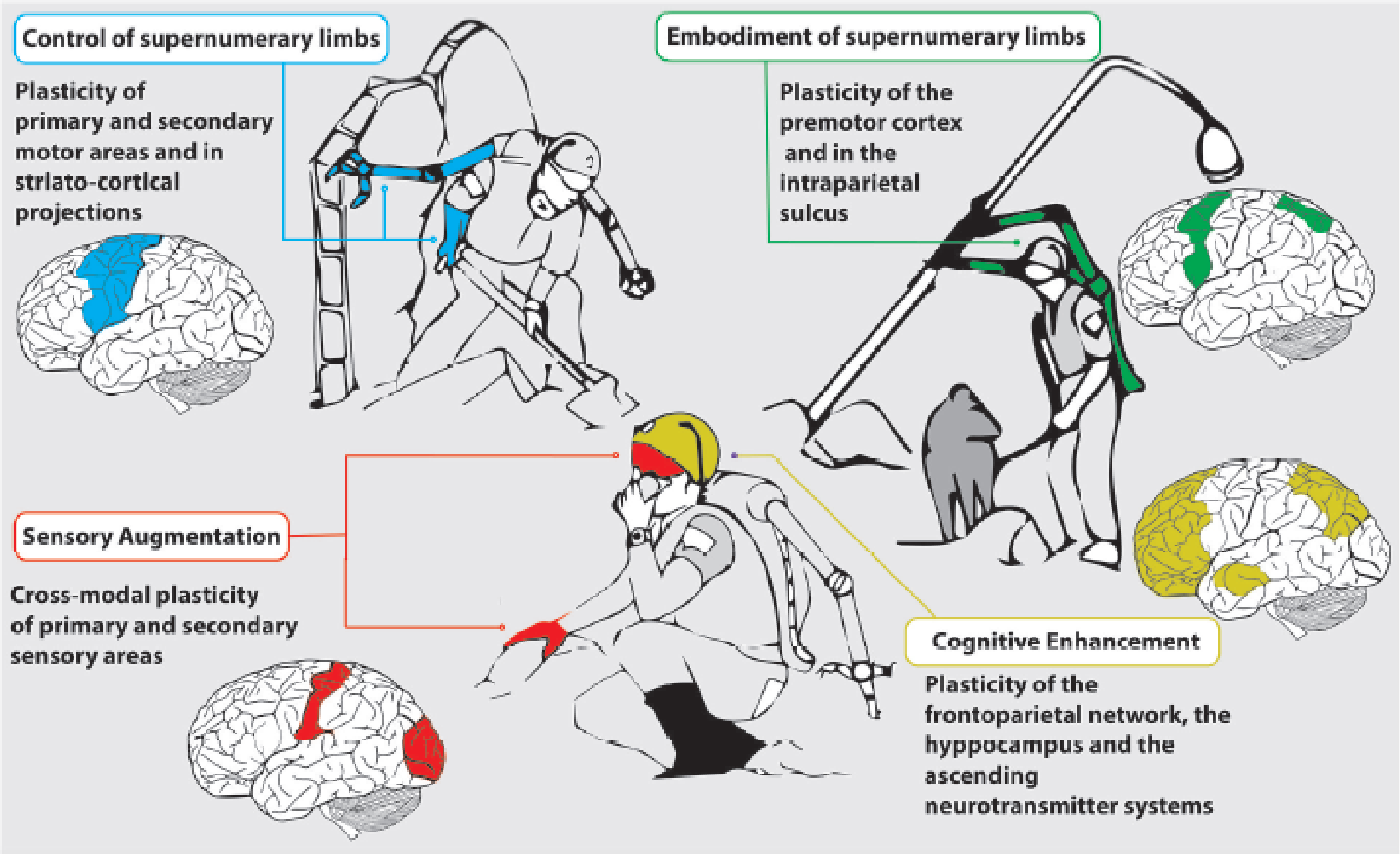


Control of supernumerary limbs

Plasticity of primary and secondary motor areas and in striato-cortical projections

Embodiment of supernumerary limbs

Plasticity of the premotor cortex and in the intraparietal sulcus

Sensory Augmentation

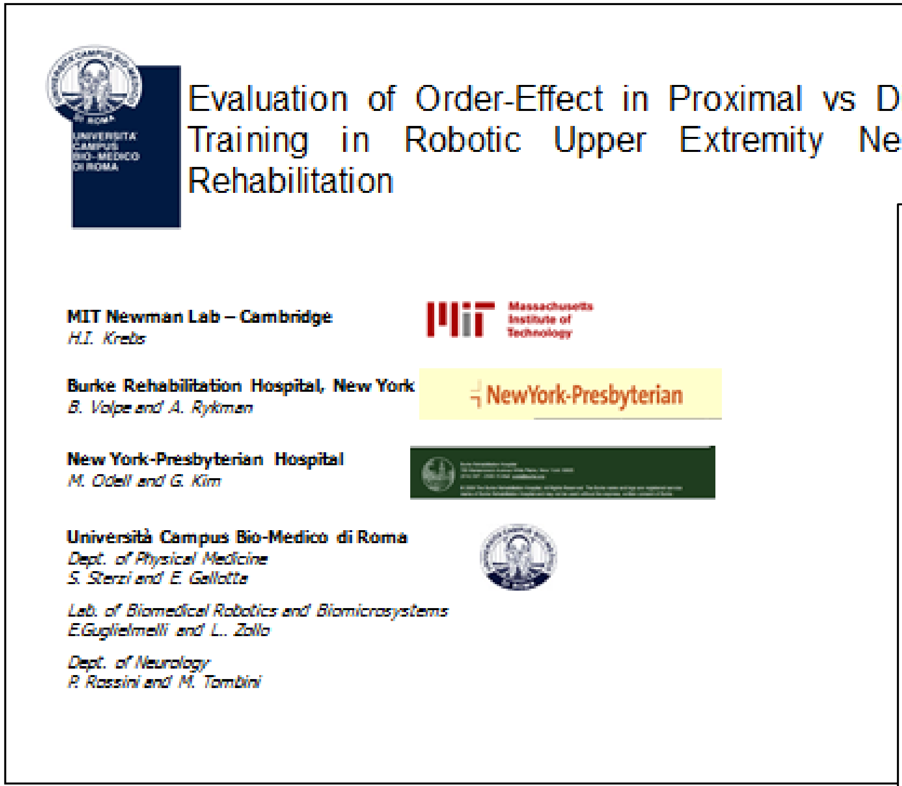
Cross-modal plasticity of primary and secondary sensory areas

Cognitive Enhancement

Plasticity of the frontoparietal network, the hyppocampus and the ascending neurotransmitter systems

Trials multicentrici

Multicentre clinical trial
Preliminary Results



Evaluation of Order-Effect in Proximal vs Distal Training in Robotic Upper Extremity Neuro-Rehabilitation

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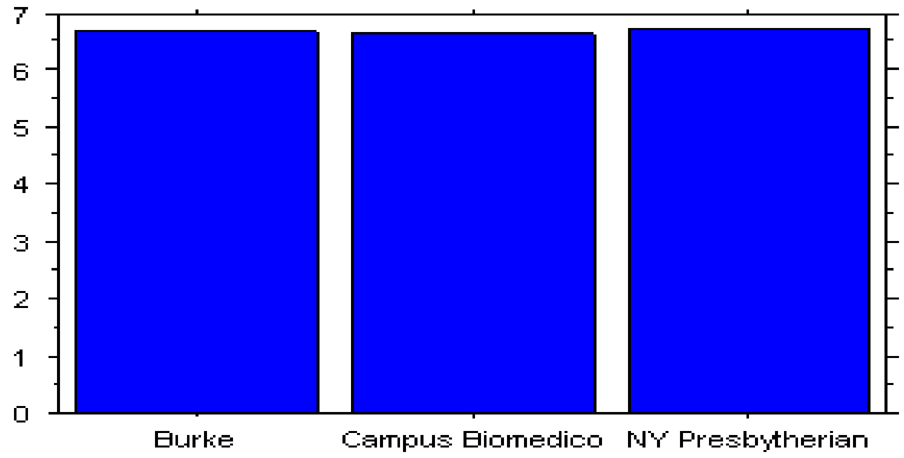
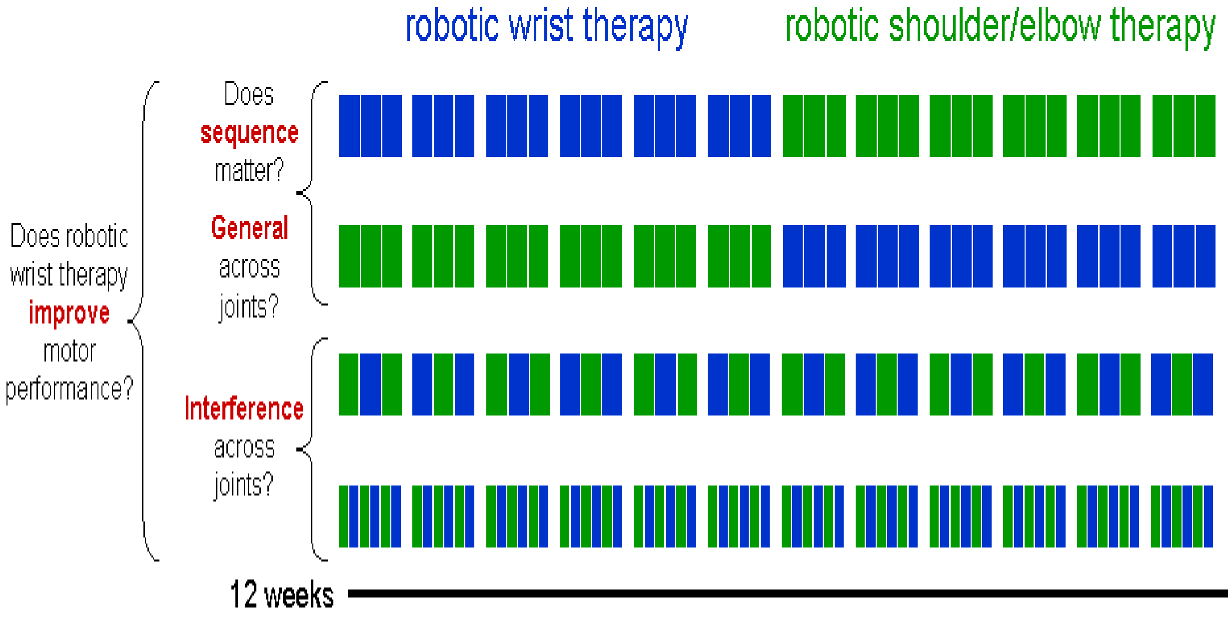
Guadagno FM-UE al termine del trial nei tre centri di ricerca



FM changes at discharge

Protocollo di sperimentazione



robotic wrist therapy

robotic shoulder/elbow therapy

Does robotic wrist therapy **improve** motor performance?

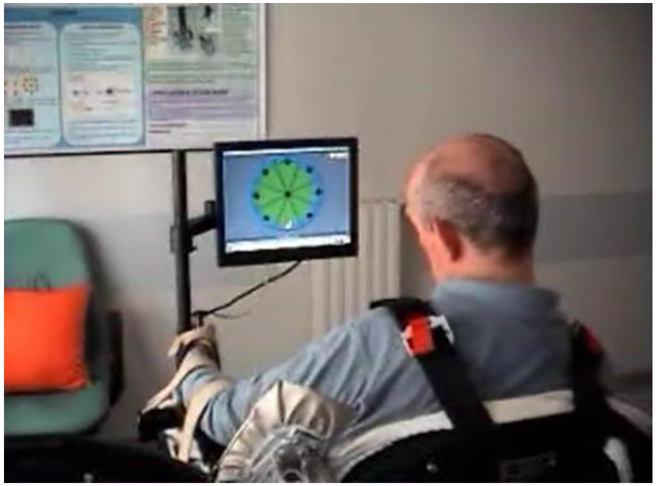
Does **sequence** matter?

General across joints?

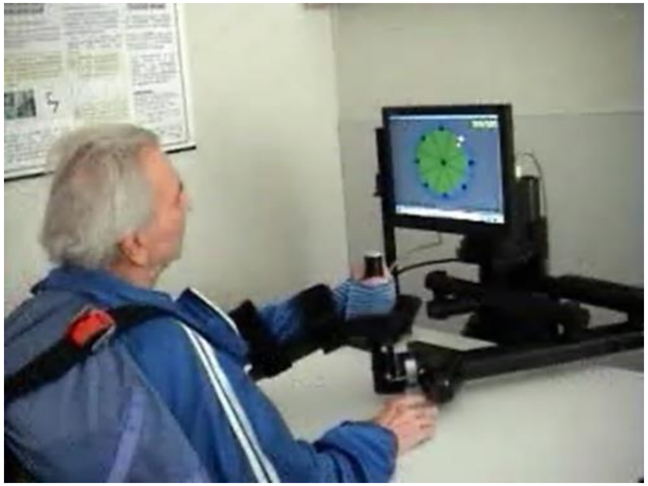
Interference across joints?

12 weeks

Group A: 6 weeks wrist - 6 weeks shoulder/elbow
Group B: 6 weeks shoulder/elbow - 6 weeks wrist
Group C: 12 weeks alternating wrist and shoulder/elbow daily
Group D: 12 weeks alternating wrist and shoulder/elbow in the same session



robotic wrist therapy



robotic shoulder/elbow therapy

Conclusioni

✓ esiste un certo grado di *interferenza*: essa si verifica nel gruppo D in cui, concentrando in un’unica sessione il trattamento di entrambi i distretti, si deprime il recupero motorio globale dell’arto superiore paretico;

✓ esiste una generalizzazione e si tratta di una *generalizzazione disto-prossimale:* se questa non ci fosse, infatti, ci aspetteremmo che, al termine della prima metà di trattamento, ciascun gruppo, il gruppo A e il gruppo B, abbia un recupero esclusivamente a carico del distretto direttamente allenato, rispettivamente il distretto distale per il gruppo A e il distretto prossimale per il gruppo B;

✓ l’*ordine* di esecuzione dei movimenti e quindi la *sequenza* nell’allenamento è importante: l’approccio migliore è quello utilizzato nel gruppo A nel quale si inizia con l’allenamento del distretto distale, polso-mano, per poi passare, nella seconda metà di trattamento, ad allenare il distretto prossimale spalla-gomito.