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Combination of Brain–Computer Interface Training and Goal-Directed Physical Therapy in Chronic Stroke: A Case Report

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Abstract

Background. There is no accepted and efficient rehabilitation strategy to reduce focal impairments for patients with chronic stroke who lack residual movements. *Methods*. A 67-year-old hemiplegic patient with no active finger extension was trained with a brain–computer interface (BCI) combined with a specific daily life–oriented physiotherapy. The BCI used electrical brain activity (EEG) and magnetic brain activity (MEG) to drive an orthosis and a robot affixed to the patient's affected upper extremity, which enabled him to move the paralyzed arm and hand driven by voluntary modulation of μ-rhythm activity. In addition, the patient practiced goal-directed physiotherapy training. Over 1 year, he completed 3 training blocks. Arm motor function, gait capacities (using Fugl-Meyer Assessment, Wolf Motor Function Test, Modified Ashworth Scale, 10-m walk speed, and goal attainment score), and brain reorganization (functional MRI, MEG) were repeatedly assessed. *Results*. The ability of hand and arm movements as well as speed and safety of gait improved significantly (mean 46.6%). Improvement of motor function was associated with increased μ-oscillations in the ipsilesional motor cortex. *Conclusion*. This proof-of-principle study suggests that the combination of BCI training with goal-directed, active physical therapy may improve the motor abilities of chronic stroke patients despite apparent initial paralysis.

Keywords

stroke, brain–computer interface, physical therapy

Introduction

Success of rehabilitation of patients with severe hemiparesis after stroke is limited. Chronic patients without active movement capacities are usually excluded from studies that examine the efficacy of rehabilitation programs. New technologies such as the development of brain–computer interfaces (BCIs) that use neurophysiological or metabolic brain activity to drive external devices offer new and promising strategies to modulate neuroplasticity and behavior in stroke survivors.[1-4]

Feedback and reward are the main aspects of motor learning.[5-8] Without any movement capacities left, feedback and reward are reduced or absent. A recently developed BCI system enables chronic stroke patients to control their μ-rhythm oscillations and drive peripheral devices. These oscillations can be recorded over the sensorimotor cortex within a frequency band of 8 to 15 Hz and its harmonics around 22 Hz during rest and disappear during actual or imagined movements. By manipulating the μ-rhythm voluntarily a mechanical orthosis affixed to the paralyzed hand can be controlled, and opening and closing of the hand is learned.[2,3] Comparable with physiotherapy in which patients' paretic limbs are passively moved while they are asked to imagine the active movement simultaneously, the BCI training links movement and motor imagery by activating

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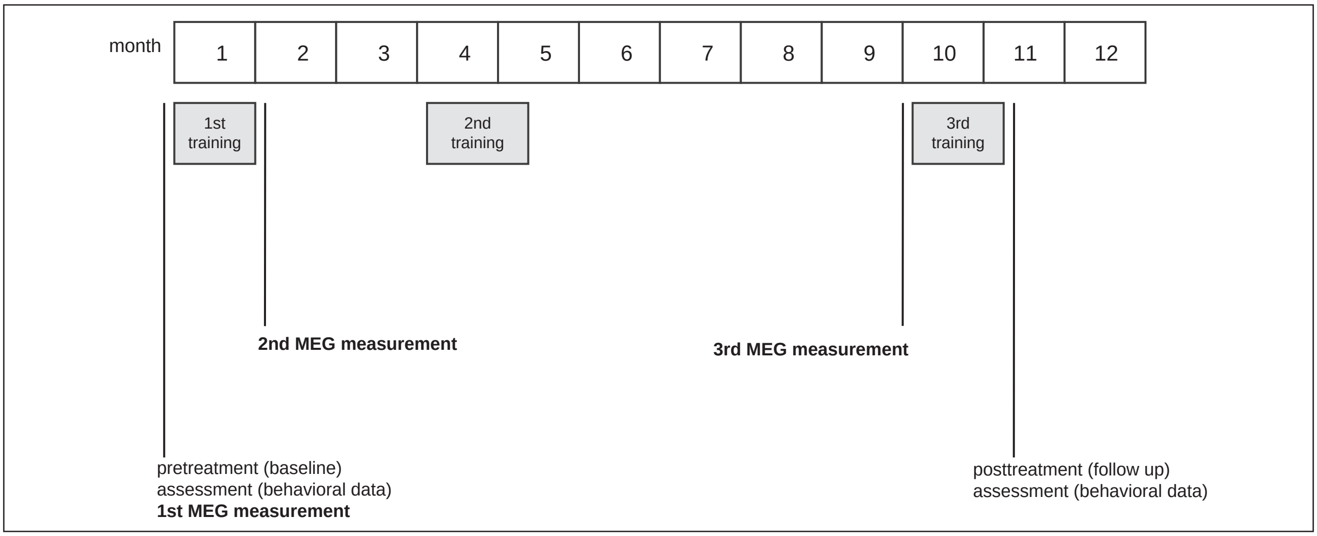

Figure 1. Schedule of BCI training, assessment of arm function and gait, and time points of magnetic brain activity measurements across 1 year

and deactivating the hand orthosis depending on μ-rhythm activity. μ-Rhythm is generally related to inactivation of the motor system.

Specific physical therapy approaches are useful for the treatment of specific disabilities in stroke patients.[9,10] Physical therapy alone, however, did not show any lasting positive effect on chronic stroke.[11] Here, we report an approach that uses a combination of BCI training and a goal-oriented active physical therapy adapted to the BCI training to transfer rehabilitation of hand movement from the lab to the patient's social environment.

Patient and Methods

The participant was a 67-year-old hemiparetic man suffering from chronic stroke after a right-sided thalamic bleeding 14 months prior to study entry. He depended on assistance for personal hygiene and dressing. He could not drive a car, and he walked slowly and with a stabilizing orthosis on his left ankle joint, always with the aid of a cane. The patient never walked over uneven ground such as grass. He used a wheelchair for all distances greater than 1000 m. During walking, spasticity brought his arm in flexion in front of the trunk. He could not extend his fingers and was unable to use his hand or arm for any relevant activity of daily living. Moreover, the paralyzed arm prevented him from standing up and walking.

Arm motor function and gait were assessed pretreatment (baseline) and after the last training period (see Figure 1). The Fugl-Meyer Assessment was done for the arm, and Wolf Motor Function Test functional ability, Modified Ashworth (shoulder flexion, elbow flexion/extension, forearm supination/pronation, wrist dorsal extension/palmar flexion, finger flexion/extension, and thumb abduction/adduction were measured) scale score, 10-m fastest walk speed, and goal attainment score were assessed. Cortical activation patterns during motor imagery measured by magnetic brain activity (MEG) were assessed pretreatment (baseline), after the first training block, and before the last training block (see Figure 1). Two goals were selected: one concerning the use of the hand (to take the cane with him in the paretic hand while grabbing a banister during climbing stairs) and one concerning gait (to walk over uneven ground). For each training block, the subsequent steps for goal attainment were fixed, and additional points were added to the goal attainment scale.

MEG measurements were performed to assess training-induced cortical reorganization. During MEG sessions, brain activity was measured during attempted hand opening and closing and during imagery of the same movements for both the paretic and nonparetic hands. A rest condition with eyes open served as the baseline condition. Task instructions were displayed on a screen via video projection. The execution and the imagery of movements was visually and acoustically paced by presenting the instructions "open" and "close" at a frequency of 1.25 Hz. Signals with the same pacing were presented during the rest condition to keep the sensory input constant. Five runs of rest, execution, and motor imagery were performed for each hand in each assessment session. For the hand movements, each run consisted of an instruction phase, a warning phase, and 15 cycles of hand opening and closing. During the session, brain activity and the pacing signal were continuously recorded using a whole head 275-channel magnetoencephalograph

(VSM, Port Coquitlam, Canada). Data were sampled at 600 Hz for the first and second measurements and at 2343.75 Hz during the third. During off-line analysis, MEG data were segmented into epochs of 0.580-s duration, starting with the trigger of the pacemaker indicating hand opening or closing. After applying a Bartlett window, epochs were subjected to a Fourier analysis. Spectral amplitudes of the μ-rhythm were computed for movements, motor imagery, and rest. Finally, single-trial spectra were averaged across trials. The averaging procedure included approximately 65 epochs for each measurement and task condition. To obtain an amplitude score for each hemisphere, spectral amplitudes of the left and right hemispheres were separately averaged across central and temporal sensors for each trial. To infer whether the differences found were statistically different, a 4-factorial analysis of variance was computed with the factors Phase (first MEG measurement, second MEG measurement, third MEG measurement), Condition (rest, movement, imagery), Hand (levels left and right), and Hemisphere (levels left and right). We tested whether differences found for the main effects and interactions exceeded the intertrial variability of the amplitude spectrum. Post hoc tests were done to identify the sources of statistical differences in factors with 3 levels.

Magnetic Brain Activity Brain–Computer Interface

During the first 2 weeks of the first block of rehabilitation training, a MEG-BCI system was used.[3] Amplitude modulation of the μ-rhythm was measured over the sensorimotor cortex. During BCI training, the μ-rhythm was fed back to the patient as a cursor movement on a screen. Depending on μ-rhythm activity, a hand orthosis affixed to the paralyzed hand opened or closed the affected limb.[3] The μ-rhythm over the ipsilesional motor cortex was acquired from 4 magnetic field sensors. The cluster of MEG sensors chosen as BCI controllers were identified after an initial session. Recorded data were transferred online to a BCI computer using the software platform BCI2000 (www.bci2000.org) for online analysis and feedback generation. During all BCI training sessions, a mechanical orthosis was attached to the plegic hand. Index, middle, ring, and little fingers were individually inserted into ring-like fasteners that grasped each digit at the first phalanx, and they were fixed by a screw-adjustable shoe to prevent slippage. Each fastener was connected to a plastic Bowden cable that allowed for passively controlled motion of the fingers from outside the shielded room. All fingers were moved in the same way, causing a hand grasp or opening. During each training session, the patient performed between 150 and 250 trials of a goal-oriented, visual feedback task. The task was designed to help achieve volitional control of μ-rhythm amplitude and, thus, control of the orthosis. Each trial was initiated by the presentation of a target on either the upper or lower half of the right side of a visual display. The target was a visual representation of an acceptable range of μ-rhythm amplitudes for the desired orthosis action. A square screen cursor would then begin moving at a fixed rate from left to right across the display, with the cursor feedback updated every 300 milliseconds. The vertical position of the cursor was a transformation of the recorded μ-rhythm amplitude. The goal for the patient was to volitionally modulate the μ-rhythm amplitude in such a way that the cursor made contact with the target once it reached the right edge of the screen. The BCI software maintained a history of the mean μ-rhythm amplitude estimate from each trial and assigned this to a distribution representing observations for each target (or orthosis action) condition. The classification threshold, defined as the midpoint between the means of these 2 distributions, was adaptive to account for changes in the shapes of these distributions over the course of training. At the conclusion of each trial in which the patient was successful at producing the appropriate modulation of μ-rhythm amplitude (meaning the cursor hit the target), a simultaneous change in target color (red to yellow) and orthosis action occurred, providing reinforcement. If the cursor failed to hit the target, no reinforcement was provided (meaning no orthosis manipulation of hand posture occurred).

Electrical Brain Activity (EEG) Brain–Computer Interface

During the second training block, an EEG-BCI system was used to drive a rehabilitation robot (Motorika, Israel). There were several reasons to start with MEG-BCI and continue with EEG-BCI. From our previous study,[3] we found that MEG-BCI seemed to be readily learned, so we used this first to boost training success. For widespread clinical applications, however, MEG-BCI is too costly and EEG-BCI is the only realistic alternative. Therefore, EEG-BCI is the method of choice if training is to continue in a real-life context with an affordable technology. Similar to the first block, the patient received feedback about the voluntarily controlled sensorimotor μ-rhythm from the ipsilesional cortex by a moving a cursor on a screen. The patient was instructed to imagine grasp movements of his affected arm. Depending on μ-rhythm modulation, the robot moved the affected arm forward and backward, following different direction trajectories.

Physiotherapy

After each BCI training session, 1 hour of goal-directed active physiotherapy was applied. The patient was asked to plan and imagine the same movements as during the BCI training—for example, "extend the fingers," "flex the

Table 1. Test Parameters of Motor Function

Functional Test	FMA Passive Flexibility and Pain	FMA Sensory	FMA Motor Ability	WMFT Functional Ability Subscale	Ashworth[a]	10-m Walk[a]	GAS
Baseline	37	5	13	7	8	18:18 s	−4
After 1 year	41	6	24	13	4	13:00 s	+10

Abbreviations: FMA, Fugl-Meyer Assessment; WMFT, Wolf Motor Function Test; GAS, goal attainment score.
[a]For these items, a low score equals a positive outcome. In all other measures, a high score indicates a good outcome.

fingers," and "relax". While the patient did so, the physical therapist stimulated the relevant muscles and moved the fingers and the arm passively to stimulate the somatosensory system. When a visible movement or muscle contraction was initiated by the patient, this movement was rewarded verbally and by touching the patient's arm or hand. The physical therapy included gait training, use of the hand for daily relevant actions (eg, grasp the stick with the affected hand during climbing the stairs), and relaxation of the arm during walking. The physical therapist guided the movements so that most exercises ended in a successful experience. Walking was included in the physical therapy concept because movement skills of the upper and lower extremity are related (eg, spasticity of the paralyzed arm increases during walking). We hypothesized that improved walking would improve arm function and vice versa. The patient continued to exercise at home every day for 1 hour, which included active finger extension and flexion; arm movements; walking; holding, carrying, and releasing his stick; and opening and closing doors with the paralyzed hand. He received a training plan that included photographs of the exercises.

Results

Behavioral Data

Follow-ups may have been very informative after each intervention. However, we were interested in long-term effects only, and the large number of independent variables involved in outcome measures in the different treatment modalities do not allow isolation of the relevant independent variables. Therefore, we decided to perform premeasurement and postmeasurement only.

All test parameters of motor function improved substantially in the time course of 1 year (Table 1). After the 3 training blocks, the patient was able to extend his fingers and to open his affected hand to grasp (eg, his stick during climbing the stairs or to shake hands). He could open and close a door with his affected hand. The arm did not spontaneously take a flexor and adduction posture and rarely disturbed activities like standing up and walking. Furthermore, the patient was able to actively relax his finger, wrist, and elbow flexors.

The patient walked safely over even ground, with and without a stabilizing orthosis or a stick. He walked regularly over uneven ground for distances of more than 1000 m. He no longer depended on assistance for personal hygiene and wearing clothing. In addition to these motor task improvements, concentration and participation also increased, demonstrated by his ability to drive a car again.

Functional Data: Changes in Spectral Amplitude of MEG

Any effect of the rehabilitation training on brain activity should be reflected by changes in cortical activity from the first to the second or the third MEG measurement. Changes should be especially obvious during the use of the paretic hand. In fact, statistical analysis of the spectral amplitude of MEG revealed a significant interaction between Phase and Hand [$F(2, 1277) = 38.842$; $P < .001$]. Moreover, a significant 3-way interaction for Phase × Hand × Hemisphere [$F(2, 1277) = 4.195$; $P = .015$] suggested a stronger change in the ipsilesional hemisphere.

According to subsequent post hoc tests, the spectral power of μ-rhythm activity (10 Hz) increased significantly at the lesioned hemisphere following the first 2-week training block [$F(1, 416) = 339.8$; $P < .0001$]. The increased μ-rhythm amplitude also remained stable during the third measurement [$F(1, 446) = 265.9$; $P < .0001$], as shown in Figures 2 and 3. As indicated by a significant main-effect Condition, movement execution and motor imagery both resulted in a significant reduction of μ-rhythm synchronization in general, that is, event-related desynchronization [$F(2, 1277) = 11.69$; $P < .0001$]; μ-amplitude for rest = 77.24 fT/Hz$^{1/2}$; movement = 75.80 fT/Hz$^{1/2}$; and imagery = 72.80 fT/Hz$^{1/2}$.

Discussion

The use of a BCI system in combination with goal-directed physical therapy improved motor function. For patients without residual function, the BCI training in combination with goal-directed active physical therapy seems to create favorable conditions to induce neuroplasticity with the aid of visual (brain-controlled cursor movements on the display) and somatosensory (proprioceptive input during orthosis-supported hand movements) feedback. To transfer

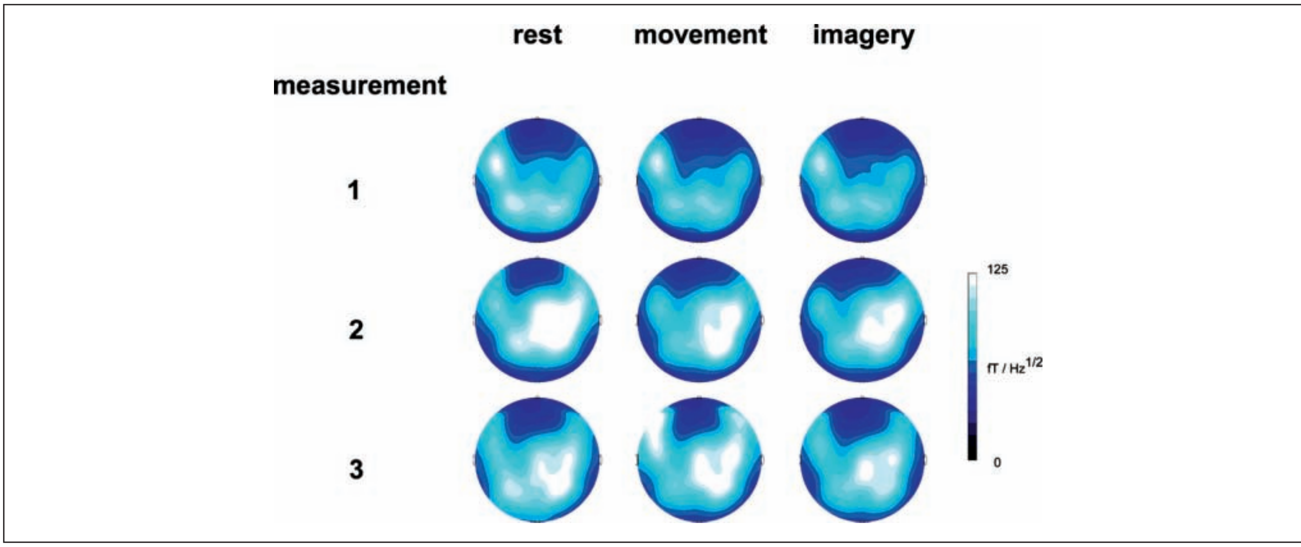

Figure 2. Changes of electromagnetic μ-rhythm amplitudes from the first measurement prior to any brain–computer interface training and the second and third measurements after training: topographic maps of μ-rhythm (top views) are shown for rest (left column) as well as for execution of paretic hand movements (middle column) and imagery of movements of the paretic hand (right column). An increase in spectral amplitude can be seen on the right, lesioned hemisphere across measurements

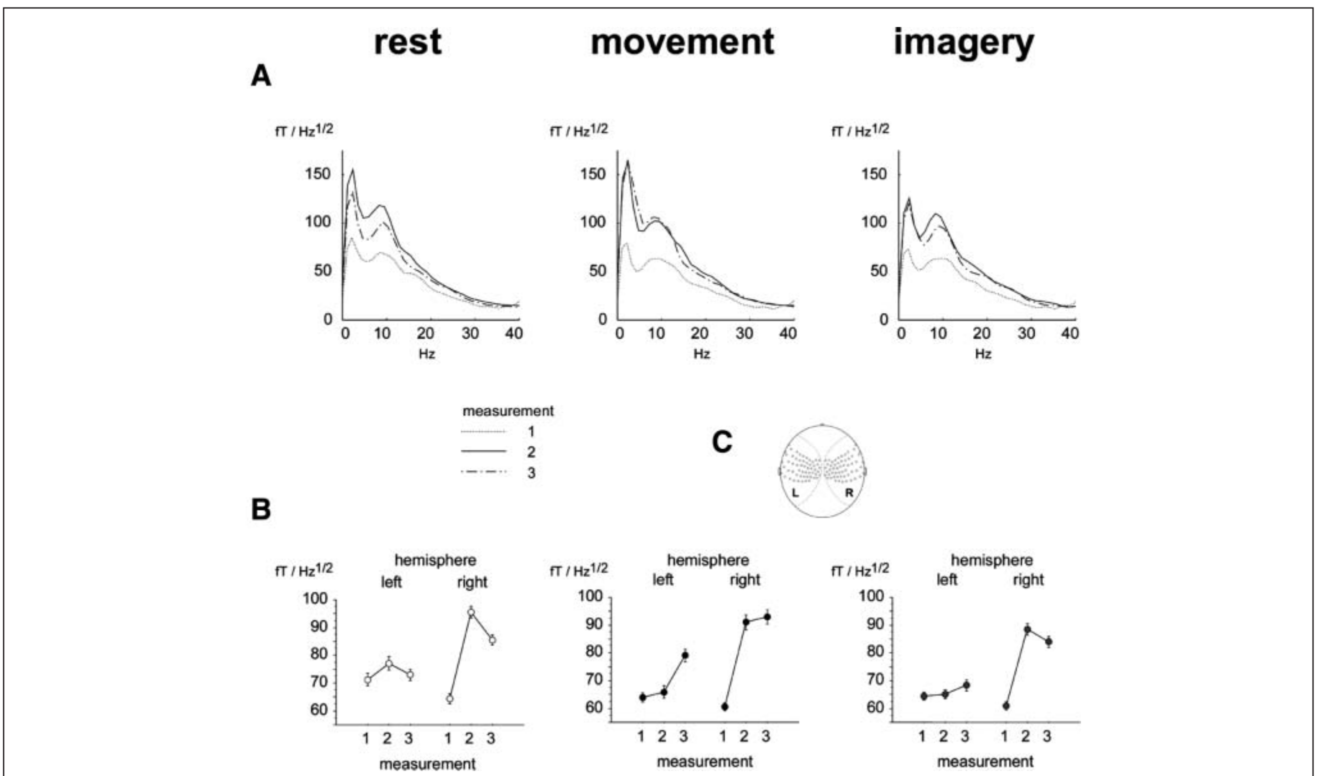

Figure 3. Spectral amplitudes of magnetic brain activity frequency spectrum for movements involving the left impaired hand: spectral amplitudes were defined as an average of the activity across a subset of sensors on the central left and right hemispheres. (A) Spectral amplitudes of the lesioned hemisphere for the 3 assessment dates (prior to training, after the first block of training, and after 10 months) and the 3 conditions (rest, movement, and imagery). (B) Sensors entering the average spectral amplitudes for the left (L) and right (R) hemispheres. (C) Spectral amplitude for μ-rhythm activity is shown for the left and right hemispheres; note the increase in μ-rhythm activity in the ipsilesional right hemisphere from the first to the second assessment

motor abilities from an artificial BCI environment to patients' daily-life environments, special physical therapy was used because BCI training alone had not led to real-life generalization of the improvement.[3] This uncontrolled study does not isolate the effects of the different treatment elements, particularly BCI training and multiple physical therapy interventions. The aim was to determine whether the combined approach, in a patient without residual finger extension, would improve outcomes. The evidence for the efficacy or the nonefficacy of physiotherapy after stroke in such patients is limited, mainly because of methodological deficits.[11] Only 1 study is available on BCI training in chronic stroke without residual movement; here, BCI training did not result in lasting behavioral changes outside the laboratory.[3] Frequent (every 2 weeks) supervision and encouragement were necessary to avoid negation of training success. Even after effective restoration of function immediately after physiotherapy, such as repetitive task training, follow-up measures were not significant for any outcome at 6 months in a large study.[12] Using functional imaging methods, the effects of BCI training on brain activation were demonstrated. Following the training, μ-rhythm activity was increased in the lesioned hemisphere. Although the patient succeeded in controlling μ-rhythm activity of the lesioned hemisphere for hand closing and opening during the BCI-assisted training, no clear lateralization of μ-rhythm activity contralateral to the active hand, as observed in healthy participants, could be documented. Since μ-rhythm is generally related to inactivation of the motor system, it might well be that the training-induced increase in μ-rhythm amplitudes is directly related to the reduction of spasm in the paretic hand and reactivation of brain areas close to the session, as predicted in the literature.[13] Despite the positive relationship between increased ipsilesional μ-power and the motor improvement, single-case data of this kind are only supportive. However, the ipsilesional reorganization with increased brain activity and remarkable improvement as found in this patient suggests that the combination of BCI technology and goal-directed active physical therapy may further improve the effects in limited reports of BCI[3] and constitute a testable rehabilitation intervention for chronic stroke survivors who lack residual finger extension.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the authorship and/or publication of this article.

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