



Research article

Effects of the multisensory rehabilitation product for home-based hand training after stroke on cortical activation by using NIRS methods

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ABSTRACT

Objective: This study aimed to assess the effects of the multisensory rehabilitation product for stroke patients on cortical activation response through near-infrared spectroscopy (NIRS).

Methods: The music rehabilitation glove (MRG), multisensory rehabilitation product, was developed with a user-centered design concept. The 40-channel NIRS system monitored the cortical activation changes in the motor cortex (MC), prefrontal cortex (PFC), temporal lobe (TL) and occipital lobe (OL) of 22 young subjects during "sequential finger-to-thumb opposition movements (SFTOM)" phase of traditional training and "musical finger-to-thumb opposition movements (MFTOM)" phase of MRG training.

Results: The two phases of training showed significant activation ($P < 0.05$) in the cerebral cortex compared with baseline, with more activation during MFTOM in the MC, PFC and TL. Compared with SFTOM, there were 22 channels of cortical activation in MFTOM that had significant enhancements ($P < 0.05$). There was also a significant positive correlation between the prefrontal cortex and motor cortex in the cortical activation.

Conclusions: According to these results, MFTOM-induced cortical activation in the MC, PFC and TL with visual, auditory and tactile stimuli was stronger than SFTOM, providing evidence that the multisensory stimulation is more beneficial to cortical activation and cognitive control to promote neurological recovery.

1. Introduction

There are approximately 795,000 and 2,400,000 new stroke patients each year in the USA and China, respectively [1,2], and 80 % of stroke patients suffer varying degrees of hand function impairment [3]. Such impairments seriously affect patients' activities of daily living (ADLs) and quality of life and, thus, hand rehabilitation has become a main goal of stroke rehabilitation. The human motor system can restore its function by enhanced, repeated rehabilitation training [4]. Nevertheless, due to cost, time, and distance, intensive treatments by therapists are usually limited and patients must continue hand function training at home.

Multisensory stimulation provided by an enriched environment can regulate a variety of biological mechanisms that enhance brain plasticity and recovery of function after stroke more effectively than standard

rehabilitation environments through cognitive, sensory, and motor stimulation [5,6]. Meanwhile, converging evidence also suggests multisensory benefits at the behavioral level [7,8]. Music, which can provide motivation and real-time feedback [9], has a close relationship with emotion [10]. Adding music to treatment can improve the exercise function of stroke patients and can increase their attention, cognition and happiness [10,11], which is a usual multisensory stimulation method [12]. Several music-based multisensory household stroke hand recovery devices have been developed, such as Kirk's home percussion instruments device [13] and Zondervan's musical gloves device [14]. However, these products are cumbersome, expensive and not portable.

The most important goal of stroke rehabilitation is to promote the recovery of the brain's neural network, thereby restoring the patient's motor function [15]. The basic principle of brain rehabilitation is based on the manipulation and regulation of external stimuli, which induces

Abbreviations: MRG, music rehabilitation glove; PFC, prefrontal cortex; MC, motor cortex; TL, temporal lobe; OL, occipital lobe; LPFC, left prefrontal cortex; RPFC, right prefrontal cortex; LMC, left motor cortex; RMC, right motor cortex; LTL, left temporal lobe; RTL, right temporal lobe; LOL, left occipital lobe; ROL, right occipital lobe; SFTOM, sequential finger-to-thumb opposition movements; MFTOM, musical finger-to-thumb opposition movements; BMC, bilateral motor cortex

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activation of the cerebral cortex [16]. Multisensory rehabilitation products lead to greater improvements in hand function recovery after long-term training, from peripheral effects and subjective aspects [14,17]. However, they do not provide objective measurement data, nor do they provide real-time online assessment and little is known about the short-term effects on cortical activation during use. Therefore, the most important challenge is assessing the effects of multisensory stimulation on the cortical activation response, which contributes to provide a targeted reference for stroke rehabilitation training and product design.

Recently, functional Magnetic Resonance Imaging (fMRI), Positron Emission Tomography (PET), and Near-Infrared Spectroscopy (NIRS) have proven to be useful in cortical activation studies [18,19]. NIRS is an optical method and non-invasive method for accurately detecting changes in cerebral blood oxygen during human exercise [20]. It relies on specific laser wavelengths (usually between 700 and 1700 nm) to monitor neural activity in the brain by measuring changes in the concentration of oxygenated hemoglobin (HbO) in the cerebral blood vessels. Compared with other methods, NIRS has advantages in its anti-jamming capability and portability and is thus suitable for this study.

In this study, we developed a music rehabilitation glove (MRG), multisensory rehabilitation product, that used visual, auditory, and tactile stimuli to help users complete hand function training without the need for external terminals. Cognitive processing is primarily performed in the prefrontal cortex (PFC), and the motor cortex (MC) plays a crucial role in sensory and motor control [21]. The occipital lobe (OL) is important in visual processing [22], while the temporal lobe (TL) mainly processes auditory information [23]. This study used NIRS to record HbO signals continuously in the PFC, MC, TL, and OL during training. Compared with the matched traditional rehabilitation training (unisensory stimulation), we hypothesized that MRG training (multisensory stimulation) would induce greater activation of the cerebral cortex and increase cognitive control more, activate the original neural pathway, and promote the recovery of exercise function.

2. Material and methods

2.1. Subjects

A total of 22 healthy subjects (11 males, 11 females) with no history of neurological, physical, or psychiatric illness were recruited for this study. The research was conducted at the Design Research Laboratory of the School of Mechanical Engineering, Shandong University. All subjects agreed to participate and signed informed consent forms. The experimental methods were approved by the Shandong University Human Ethics Committee and implemented according to the ethical standards of the 1975 Helsinki Declaration (revised in 2008). Table 1 summarizes the characteristics of the subjects.

2.2. Devices

2.2.1. Design development

In this study, questionnaires, user interviews, and field research were used to investigate the users' behaviors and experiences. Then, an

Table 1
Characteristics of the subjects.

	Subjects(N = 22)
Sex(male/female) ^a	11/11
Age(years) ^b	24.41 ± 2.085
Height(cm) ^b	169.48 ± 7.56
Weight(kg) ^b	62.96 ± 14.15
Dominant arm(right/left) ^a	21/1

^a Absolute numbers.

^b Mean ± standard deviation.

Table 2

Design requirements of the Hand rehabilitation product.

Characteristic	Requirements
User requirements analysis	
Rehabilitation guidance	Simple and effective standard rehabilitation ; Complete the action according to the system prompt ; Training time:45 min/d ;
Functional training	Keep fun, provide entertainment and recognize achievement during training ; Hand flexibility, strength and coordination training ; Know the training plan and completion level ;
UE (user experience)	Good man-machine experience ; Interesting psychological experience ; Natural and simple interaction ;
Wearable mode	Easy-to-wear semi-wrapped structure;
Fixed mode	Velcro (easy to adjust);
Finger fixation mode	Set into the whole finger
Interactive mode	Lights, sounds, touching
Practical considerations	
Practical consideration	Safe, portable, anti-torque ; Lightweight, well-adapted ; Low-cost, long battery life ;
Control and realization	Open-source electronic prototype platform

affinity graph was used to analyze and summarize the research content to identify user needs. The design requirements obtained from a literature review and the user research are summarized in Table 2.

The MRG was selected as the final design. Finger-to-thumb and pinch movements, which are the effective hand functions for rehabilitation training, were selected as rehabilitation actions. Daily tasks can be described in nine different synergies [24]. The seven movements of the MRG (Fig. 1A) contain six of the nine major synergies of the standard rehabilitation actions applicable to daily activities.

2.2.2. MRG (Multisensory rehabilitation product)

The functional prototype of the MRG (right hand) has, in total, seven sensor switches on the fingertip of the four fingers (except the thumb) and the middle segment of the index, middle, and ring fingers (Fig. 1). These switches represent the seven notes of Do, Re, Mi, Fa, Sol, La, and Ti. Each switch controls the high, medium, and low sounds of the note. The back of the MRG comprises a 1.5-mm-thick flexible plastic sheet and 2.5-mm-thick artificial leather (Fig. 1B). The finger part is a sports glove without the palm and the thumb. A flexible plastic sheet is fixed on the back of each finger and connected to the back of the MRG with a tension spring of 0.5 mm (wire diameter) x5 mm (outer diameter) x30 mm (length). The resistance can be adjusted by changing the specifications of the tension spring (Fig. 1C). The wrist and palm are fixed with Velcro, which can be adjusted to suit different hand sizes. The Arduino control section is placed externally to reduce the glove's weight. The Arduino-UNO development board was selected for the hardware and the Arduino IDE (V1.5.7) was used for the software development environment, which can replace the music score. The sensor switches use tact switches and light-emitting diodes. When on, the diode emits blue light, guiding the thumb and the corresponding switch to perform the finger-to-thumb or pinch movements. The duration of the notes depends on the duration of pressing the switch, with the shortest duration being 300 ms. The power supply uses a 9-V rechargeable battery. The sound module uses the Arduino 3.5-mm audio module with external headphones.

Users need to use their thumb and the lighted switch of the seven switches to perform the finger-to-thumb or pinch movements to complete the training. The glove's sound module plays a corresponding note simultaneously. As the time of action increases, the notes can be linked with songs selected by users to motivate users to continue training.

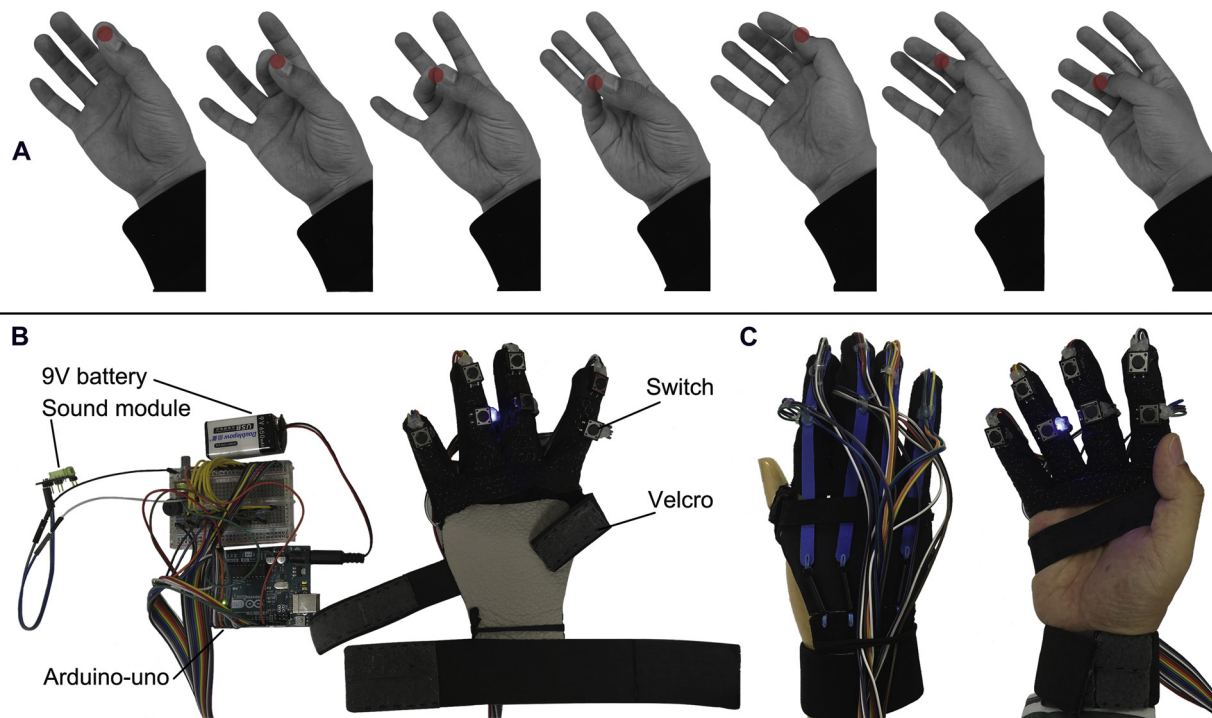


Fig. 1. (A) Seven different hand movements related to the music rehabilitation glove, from left to right: finger-to-thumb movement of the thumb and index, middle, ring, and little fingers; pinch movement of the thumb and the middle segment of the index, middle, and ring fingers. (B) Functional prototype of the MRG (right hand) and all the components of the MRG. (C) Back and working state of the MRG.

2.3. Experimental procedure

The experiment had two phases: 520 s of "sequential finger-to-thumb opposition movements" (SFTOM) and 520 s of "musical finger-to-thumb opposition movements" (MFTOM). The SFTOM phase was the matched traditional (unisensory) training and the MFTOM phase was the MRG (multisensory) training. Before each experiment, subjects were familiarized with the equipment operation and the tasks of each phase. The two phases were separated by 8 min to eliminate error effects.

During the experiment, all subjects were asked to sit comfortably and place their right hand on a table. The subjects wore MRG, headphones (Sony Mdr100abn), and NIRS devices. To control the variables, subjects also wore the MRG during the SFTOM, but it did not work. First, the subjects underwent SFTOM. Subjects rested for 20 s, then executed the block paradigm (i.e., moved right hand for 30 s, then had a rest for 20 s), which was repeated ten times. All subjects performed the test under the guidance of the "move right hand" and "rest" slogans on the computer. The "move right hand" instruction asked subjects to use the thumb and seven switches in a counter-clockwise order to perform the finger-to-thumb and pinch movements. "Rest" instructed subjects to stop moving. The MFTOM began 8 min after the end of the STFOM; the MRG worked normally during the MFTOM. Except for "move right hand", the subjects needed to use their thumbs to perform the finger-to-thumb or pinch movement with the lighted switch, successively; all other experimental requirements were the same as for the SFTOM. The MRG contained four pieces of music, which were looped: "City of the Sky", "Birthday Song", "Ode to Joy", and "Mom is the Best in the World". In total, the music contained 337 notes. The entire experiment maintained a quiet environment and did not require the frequency and amplitude of the movements.

Subjects needed to complete the Intrinsic Motivation Inventory (IMI) after the experiment to obtain their subjective perceptions. This research selected 22 questions from a total of 45 questions of the IMI to quantify motivation. These questions were divided into five subsets:

Interest/Enjoyment, Perception Competence, Effort/Importance, Pressure/Tension, and Value/Usefulness.

2.4. NIRS data acquisition

The device for detecting HbO signal changes was a multi-channel, commercial, near-infrared system (Nirxmart, Danyang Huichuang Medical Equipment Co. Ltd, China), which was used in previous studies [22,25]. The sampling frequency was 10 Hz. The wavelengths were 760 and 850 nm. Based on the international 10/20 system, 40 SD probes (consisting of 24 sources and 16 detectors) were placed in the right prefrontal cortex (RPFC), left prefrontal cortex (LPFC), right motor cortex (RMC), left motor cortex (LMC), right temporal lobe (RTL), left temporal lobe (LTL), right occipital lobe (ROL) and left occipital lobe (LOL), to form 40 channels of NIRS (Fig. 2).

2.5. Data preprocessing

The NirSpark software package, run in MATLAB (The Mathworks, USA), was used for analyzing NIRS data. Data preprocessing was divided into six steps: eliminating the time interval unrelated to the experiment; removing the artifacts unrelated to the experimental data; converting the light intensity to optical density; choosing the band-pass filter (0.01–0.2 Hz) for the noise and interference signals to filter; converting optical density into blood oxygen concentration; setting the hemodynamic response function (HRF) initial time to -2 s and the end time to 50 s (with -2 s–0 s as the reserved baseline state and 0 s–50 s as the time for a single block paradigm). With the "move right hand" duration set to 30 s, the blood oxygen concentration of the 10 block paradigms was superimposed and averaged, to generate a block average result.

2.6. Analysis of NIRS data

The generalized linear model (GLM) [26] was used to analyze the

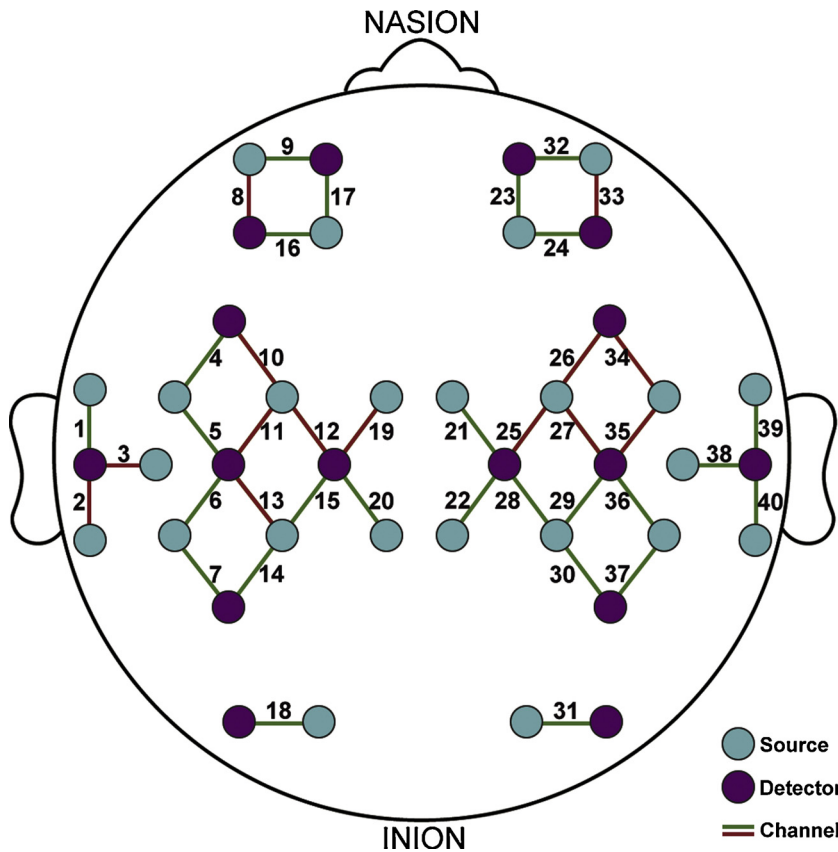


Fig. 2. Configuration of the measurement channels in the PFC, MC, TL, and OL areas according to the international 10/20 system. When comparing the cortical activation between SFTOM and MFTOM, the Wilcoxon signed-rank test was used for the red channel ($P < 0.05$) and paired-samples t -test was used for the green channel ($P > 0.05$) according to the normal distribution measured by the Shapiro–Wilk test of the paired data.

HbO time-series data, which had been pre-treated for each channel of each subject, and to perform the t -test ($P < 0.05$ between baseline and task states). The GLM could establish an ideal HRF for each task, for each subject, and then calculate the degree of matching between the experimental and ideal HRF values [27]. The beta value, which reflects the level of cortical activation of the channel, was used as an estimate of the HRF prediction of the HbO signal [28] and can be used to represent the peak value of the HRF function. The cortical activation, discussed later in this paper, is mainly based on the beta value of the channel.

2.7. Statistical analysis

Statistical analysis of the data was performed using IBM SPSS (v. 23.0). The Shapiro–Wilk test was used to determine whether the paired data of the samples conformed to a normal distribution. The paired-sample t -test was used to test for normal distribution and the Wilcoxon signed-rank test was used to test for non-conformity. Significant differences between the subjective scales of subjects were determined by using the non-parametric Wilcoxon signed-ranks test. The Spearman correlation coefficient, a non-parametric statistic, was chosen to analyze the correlation of the cortical activation between the MC and other cortices (note that only RPFC and LMC data are consistent with the bivariate normal distribution but not with the linear distribution). $P < 0.05$ was considered statistically significant.

3. Results

3.1. Analysis of intra-phase cortical activation

Table 3 shows the beta values of 40 channels after the analysis. During SFTOM, the highest beta value channel was 0.294, located in the LMC. The lowest beta value channel was -0.184 , located in the LTL. During MFTOM, the highest beta value was 0.4415, located in the LMC, while the lowest beta value was -0.0121 , located in the LTL.

Table 3

The beta values of 40 channels at each phase after the analysis.

Brain partitions	SFTOM phase			MFTOM phase		
	Number of channels	Average value	Standard deviation	Number of channels	Average value	Standard deviation
LTL	3	-0.009	0.088	3	0.046	0.053
RTL	3	-0.064	0.025	3	0.087	0.063
LPFC	4	0.044	0.022	4	0.130	0.028
RPFC	4	0.011	0.047	4	0.096	0.030
LMC	12	0.173	0.079	12	0.255	0.119
RMC	12	0.121	0.045	12	0.189	0.046
LOL	1	0.086		1	0.087	
ROL	1	0.093		1	0.136	

The number of channels represents the number of NIRS channels contained in this brain region.

Fig. 3A and B show an anatomical view of the cortical activation of the two phases presented in different colors. The higher the channel's beta value, the redder the channel; the lower the beta value, the bluer the channel.

Regardless of SFTOM or MFTOM movements, channels in the LMC showed cortical activation. When comparing the cerebral cortex activity with the baseline, during SFTOM, eight LMC and two RMC channels showed significant activation ($P < 0.05$; Fig. 3C) while during MFTOM, significant activation ($P < 0.05$) occurred in the cortex of eleven LMC, eleven RMC, three LPFC, three RPFC, and one RTL channels (Fig. 3D).

3.2. Analysis of between-phase cortical activation

Significant differences in the cortical activation between the two phases were compared with the beta values in each channel of each

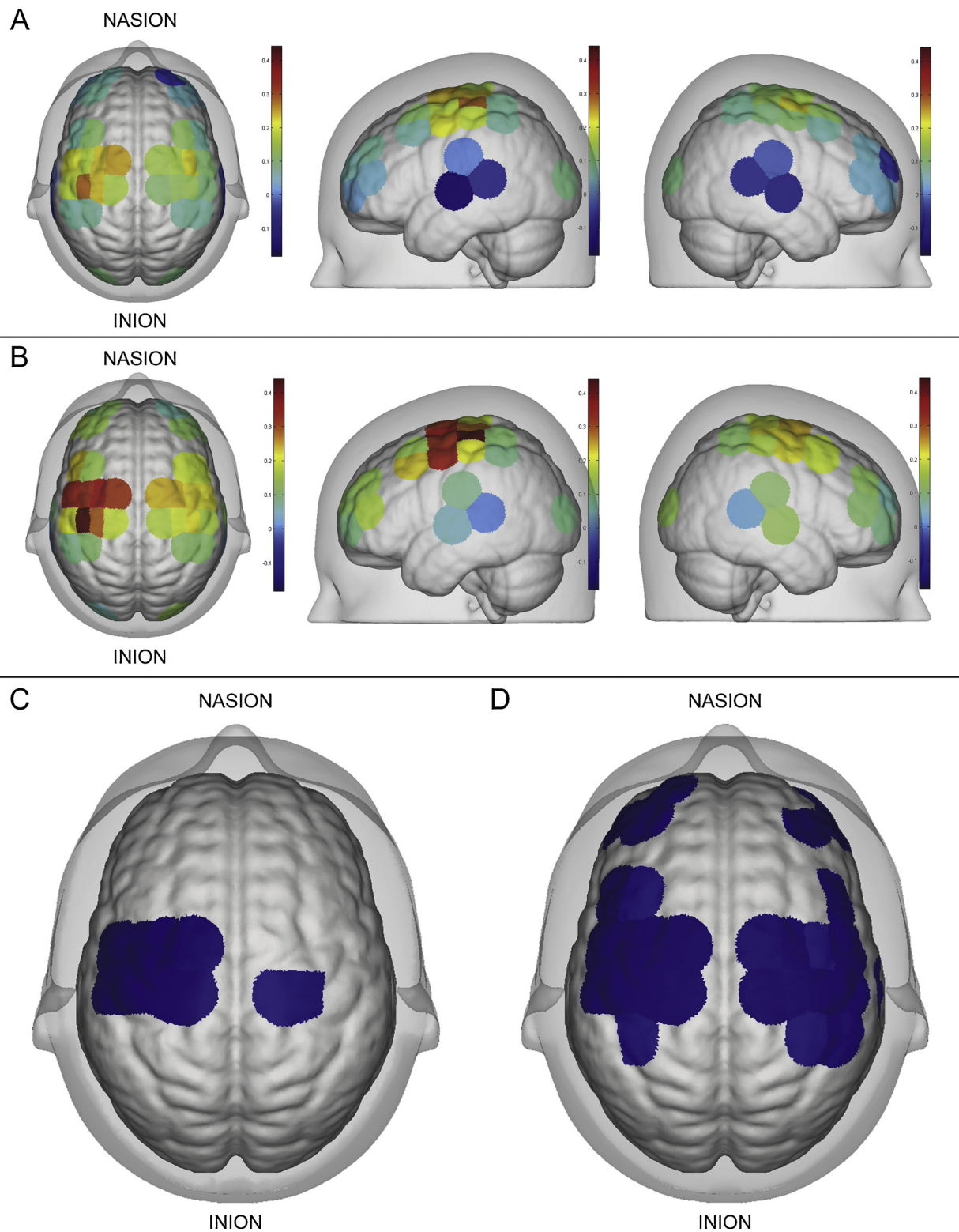


Fig. 3. (A) The activation of the cerebral cortex induced by SFTOM, (B) The activation of the cerebral cortex induced by MFTOM, (C) Significant activation of the SFTOM phase relative to the baseline. (D) Significant activation of the MFTOM phase relative to the baseline.

subject. Based on the normal distribution law of the two data sets, the green channels were tested using the paired-sample *t*-test and the red channels were tested using the Wilcoxon sign-rank test (Fig. 2). Compared with SFTOM, the MFTOM showed significant enhancements in the cortical activation in 22 channels located in LPFC, RPFC, LTL, RTL, LMC, and RMC (Table 4).

3.3. Activation correlation analysis between the motor cortex and other cortices

With respect to the PFC and MC (Fig. 4), except for a strong correlation in the cortical activation between LPFC and RMC (Spearman's Rank Correlation Coefficient, $r_s = 0.545$, $P < 0.001$). There was a

Table 4

Compared with SFTOM, channels with significantly enhanced cortical activation during MFTOM.

Cortical activation area	Channels
LPFC	8**, 16*, 17*
RPFC	23*, 24**, 33*
LTL	1**, 3*
RTL	38**, 39**
LMC	4**, 5**, 11**, 12*, 13*, 19*
RMC	26*, 27*, 29*, 34*, 35**, 36*

* $P < 0.05$ ** $P < 0.01$

moderate correlation in the cortical activation between LPFC and LMC ($r_s = 0.484$, $P = 0.001$), RPFC and LMC ($r_s = 0.353$, $P = 0.019$), and RPFC and RMC ($r_s = 0.487$, $P = 0.001$).

In the TL and MC, there was only one moderate correlation in the cortical activation between LTL and LMC ($r_s = 0.34$, $P = 0.024$). In the OL and MC, there was a moderate correlation in the cortical activation between LOL and LMC ($r_s = 0.39$, $P = 0.009$) and ROL and LMC ($r_s = 0.469$, $P = 0.001$).

3.4. Survey results

The IMI result (Fig. 5) shows the following: MFTOM was significantly more enjoyable and interesting than SFTOM ($P < 0.001$); MFTOM, with light guidance, was significantly easier to operate than SFTOM ($P = 0.032$); subjects made more effort in the MFTOM ($P = 0.001$). However, there was no significant difference in the pressure/

tension between the two phases ($P = 0.711$) with both scoring less than 50 % (total score of 7 points). Subjects also considered that MFTOM was significantly more practical and valuable than SFTOM ($P < 0.001$).

4. Discussion

This study designed a music rehabilitation glove, and created a multisensory interaction rehabilitation training mode that motivated users to complete hand rehabilitation exercises. We then investigated the cortical activation induced by the MRG using NIRS and compared it with the matched traditional rehabilitation training to reveal the effects of the multisensory stimulation on brain function. Compared with the baseline, the two phases showed significant activation of the cerebral cortex, while MFTOM induced more activation, covering the PFC, MC, and TL. Compared with the SFTOM, there were 22 channels of cortical activation that were significantly enhanced during the MFTOM and there was a significant positive correlation in the cortical activation between the PFC and MC.

Partial HbO signal variation, a common parameter of NIRS, is closely related to changes in brain neural activity [29]. It indirectly measures changes in the neural activity of the brain by detecting hemodynamic changes in the cerebral cortex [20]. The increase in neural activity can regulate blood flow, thus increasing HbO, which is referred to as neurovascular coupling [30]. Recently, the generalized linear model, which is commonly used in fMRI, has been applied to NIRS [26]. The beta value reflects the activity of the cerebral cortex and can be used to analyze related problems [27,28]. A previous NIRS study showed that using a rehabilitation robotic hand could induce cortical activation of the MC [18]. A fMRI study showed significant activation of

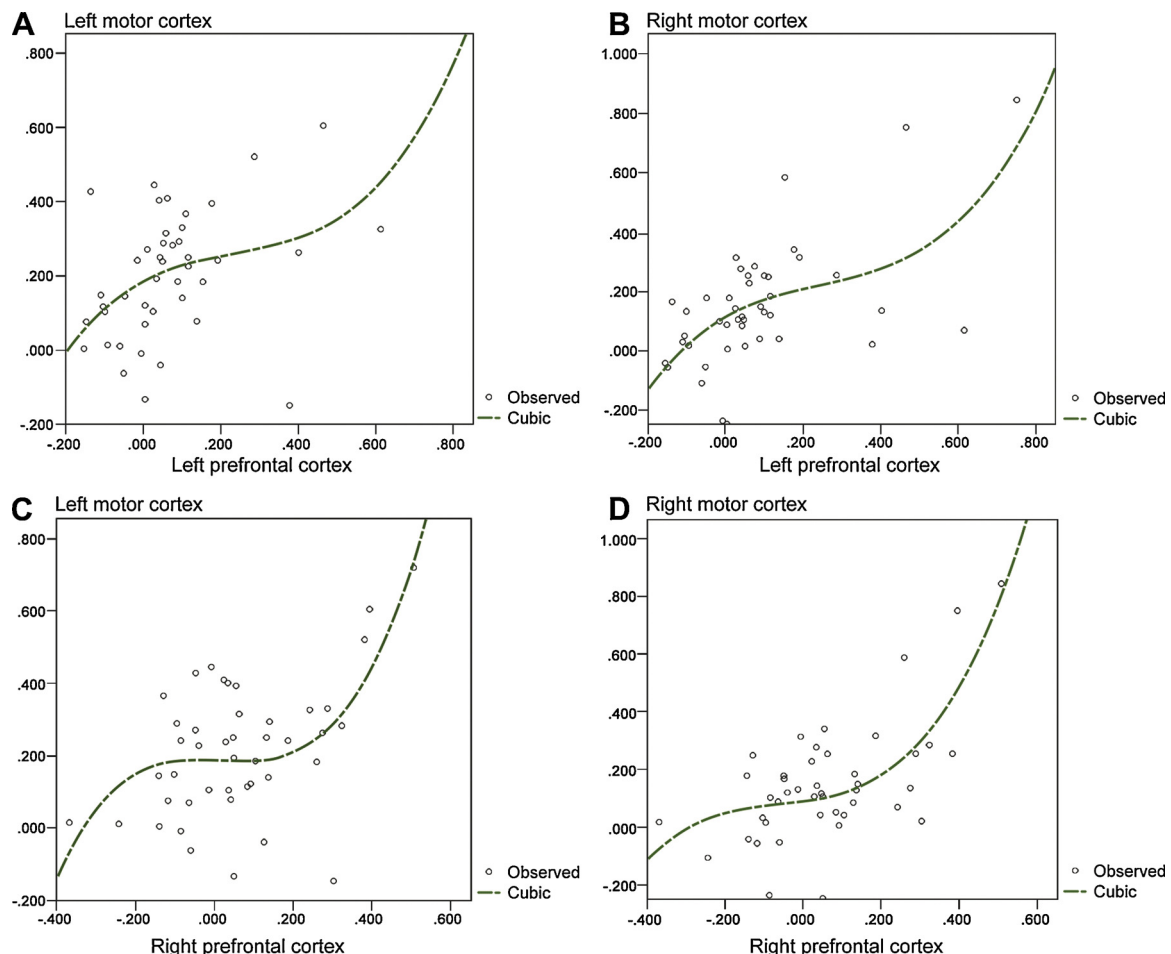


Fig. 4. The curve of the cortical activation correlation between the PFC and MC. (A) LPFC and LMC, (B) LPFC and RMC, (C) RPFC and LMC, (D) RPFC and RMC.

Intrinsic Motivation Inventory Categories

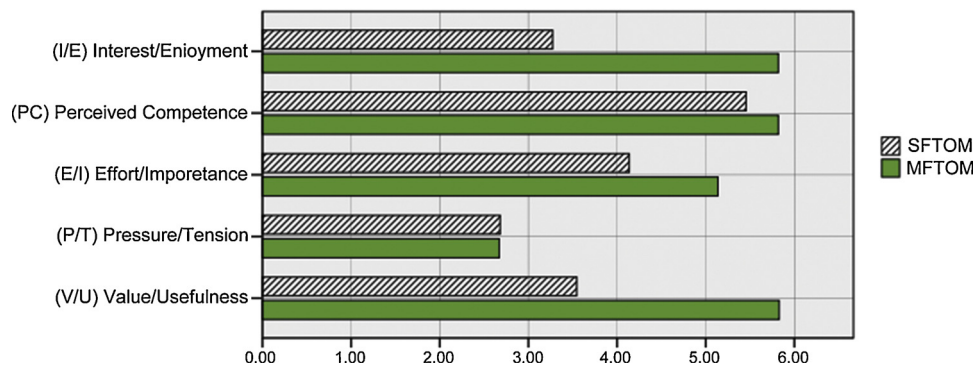


Fig. 5. Results of the Intrinsic Motivation Inventory (IMI) after the experiment with each phase. Significant differences between phases measured by the Wilcoxon signed-rank test and $P < 0.05$ was considered significant. There was no significant difference in pressure/tension between phases.

the MC of the brain, especially in the premotor cortex, when the hand completes finger-to-thumb movements in order [19]. In this study, significant activation of eight channels of the LMC and two channels of the RMC occurred during SFTOM and significant activation of eleven LMC, eleven RMC, three LPFC, three RPFC, and one RTL channels occurred during MFTOM. A functional neuroimaging study revealed that activation of the bilateral motor cortex (BMC) is induced by right-handed tactile stimulation [31]. Our data showing cross-control of motor functions is consistent with previous [31] and medical research. Owing to brain self-regulation, these phenomena may be caused by cortical blood flow changes to compensate for metabolic requirements [25].

The activation of the MC reflects the changes of HbO during bodily-kinesthetic movement, and the PFC, TL, and OL respond to specific physiological changes [21–23]. During the entire experiment, the brain activation response included not only the stimulation of hand movement but also the stimulation of other senses, such as sound and vision. Multisensory approaches to the natural environment better enable users to participate in simultaneous sensory, cognitive, and physical activities [32]. Previous studies have shown that prolonged exposure to simultaneous audio-visual stimuli can enhance activation of the cerebral cortex [8]. A fMRI study showed that visual-tactile multisensory stimulation enhances sensory motor cortex activation compared to tactile single-sensory stimulation [5]. Stroke training based on music can activate the cerebral cortex regions of sensory processing, attention, and memory [11]. Due to multisensory stimulation recruiting and in turn strengthening the residual (sensory) pathways in the brain, they can produce positive long-term effects [33]. A study found that audiovisual training improved daily living activities compared to individual visual training, and these effects remained stable for 3 months and 1 year of follow-up [34]. Our results are comparable with those of previous studies. In this study, not only did the PFC and TL participate in activities related to decision-making and executive function tasks, but they also activated the BMC during MFTOM. Moreover, compared with SFTOM, there were significant enhancements of cortical activation in 22 channels of MFTOM ($P < 0.05$), including the sensory motor cortex. We speculate that subjects would slow down the frequency and amplitude of the finger during SFTOM, or even stop, because the task is boring. In contrast, MFTOM is more likely to encourage subjects to complete the training and provide sensory feedback immediately.

However, the extent to which this encouragement occurs depends on the appropriate relationship between the senses [7]. A balanced excitatory and inhibitory ratio is the key to the brain's appropriate response to different sensory inputs. The transmission intensity and quality (such as sensory combinations and training duration) of external sensory stimulation can lead to different results of excitation and inhibition regulation [35]. In addition, when there is concordance in

multisensory stimulation in the environment, it can cause a significant increase in neuronal activity. Significantly enhanced activity is induced in multisensory neurons when two different sensory stimuli are in spatial and temporal concordance or consistent with the individual's prior experience, whereas the cortical activity is not enhanced and may even be depressed when these stimuli are discordant [36]. Our results also support these observations. MFTOM with consistent audio-visual characteristics more widely activates the cerebral cortex and the activity of neurons is significantly enhanced, which also provides a reference for future design and research.

Advanced neural information processing functions, such as analysis and critical thinking, are performed in the PFC [25]. A study has demonstrated an effective link between motor and cognitive regions during motor execution and imagery [37]. Multisensory stimuli based on music training can enhance the functional connections between the cortex [11]. This paper found a significant positive correlation in cortical activation between the PFC and MC. MFTOM-induced cognitive control indicates that the subject is more focused on training and is more motivated to perform long-term exercise. It is particularly important to note that sensory stimuli can cause brain cognition and thinking, and then cognitive control may affect behavioral performance. Moreover, most subjects believed that MRG training was more interesting, useful, and motivating for training. Interestingly, there was no significant difference in the pressure/tension scores between the two phases. SFTOM is a simple hand movement that requires no training and it also shows that the MRG is easy to operate.

The basic principles of brain rehabilitation are based on the manipulation and regulation of external stimuli that induce cortical activation [16]. In MFTOM, cortical activation is stronger than in SFTOM, which indicates that MFTOM tasks can induce the regulation and manipulation of brain treatment more comprehensively, which is beneficial to the recovery of brain function. This also indicates that multisensory rehabilitation products, like MRG, could activate the cerebral cortex more effectively which could promote the recovery of the brain's neural network. Because such products stimulate significant goal-oriented movements in users and motivate them to work harder during training through appropriate multisensory interaction.

This study utilized a mature NIRS method to reveal the effect of multisensory stimulation on brain neurons, through measuring the induced cortical activation response. Further research will recruit stroke patients to comprehensively and longitudinally verify the effects of the MRG, and to explore the optimal sensory stimulation's combination, frequency, duration, and intensity.

5. Limitations

A limitation of this study is the small number of subjects. A greater

number of subjects will, therefore, be used to verify the results in subsequent studies. Moreover, there is systematic interference in the cerebral oxygenation signal measured by NIRS and so further studies will use short-channel or spatial regression methods to avoid this interference.

6. Conclusion

The present study developed a multisensory rehabilitation product, the MRG, to help users to complete hand function rehabilitation training at home. The effect of the MRG on cortical activation was also analyzed. The cortical activation induced by MFTOM was greater and more intensive than that during SFTOM. The results indicate that multisensory stimulation can induce the activation of the cerebral cortex and promote the recovery of brain nerves more effectively. Activation of the MC also significantly positively correlated with cognitive performance. The findings will, therefore, contribute to the research and development of stroke rehabilitation products and training.

Author contributions

Qinbiao Li did the experiment, analyzed the data, and drafted the manuscript. Jian Feng and Jia Guo did the experiment. Zilin Wang analyzed the data. Puhong Li performed the statistical analysis. Heshan Liu and Zhijun Fan designed the study and edited the manuscript.

Declaration of Competing Interest

The authors have declared that no competing interests exist.

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References

- [1] E.J. Benjamin, P. Muntner, M.S.J.C. Bittencourt, Heart Disease and Stroke Statistics-2019 Update: a Report from the American Heart Association vol. 139, (2019), pp. e56–e528.
- [2] W. Wang, B. Jiang, H. Sun, X. Ru, D. Sun, L. Wang, L. Wang, Y. Jiang, Y. Li, Y.J.C. Wang, Prevalence, Incidence, and Mortality of Stroke in China: Results from a Nationwide Population-Based Survey of 480 687 Adults vol. 135, (2017), pp. 759–771.
- [3] V.M. Parker, D.T. Wade, R. Langton Hewer, Loss of arm function after stroke: measurement, frequency, and recovery, *Int. Rehabil. Med.* 8 (1986) 69–73.
- [4] L. Ada, S. Dorsch, C.G. Canning, Strengthening interventions increase strength and improve activity after stroke: a systematic review, *Aust. J. Physiother.* 52 (2006) 241–248.
- [5] H.G. Kwon, S.H. Jang, M.Y. Lee, Effects of visual information regarding tactile stimulation on the somatosensory cortical activation: a functional MRI study, *Neural Regen. Res.* 12 (2017) 1119–1123.
- [6] J. Hakon, M.J. Quattromani, C. Sjolund, G. Tomasevic, L. Carey, J.M. Lee, K. Ruscher, T. Wieloch, A.Q. Bauer, Multisensory stimulation improves functional recovery and resting-state functional connectivity in the mouse brain after stroke, *Neuroimage Clin.* 17 (2018) 717–730.
- [7] L. Shams, A.R. Seitz, Benefits of multisensory learning, *Trends. Cogn. Sci.* 12 (2008) 411–417.
- [8] N.M. Dundon, C. Bertini, E. Ladavas, B.A. Sabel, C. Gall, Visual rehabilitation: visual scanning, multisensory stimulation and vision restoration trainings, *Front. Behav. Neurosci.* 9 (2015) 192.
- [9] S. Schneider, P.W. Schonle, E. Altenmuller, T.F. Munte, Using musical instruments to improve motor skill recovery following a stroke, *J. Neurol.* 254 (2007) 1339–1346.
- [10] T. Sarkamo, M. Tervaniemi, S. Laitinen, A. Forsblom, S. Soinila, M. Mikkonen, T. Autti, H.M. Silvennoinen, J. Erkkila, M. Laine, I. Peretz, M. Hietanen, Music listening enhances cognitive recovery and mood after middle cerebral artery stroke, *Brain* 131 (2008) 866–876.
- [11] J.J. Jo.P.-C. Strzemecka, C. Research, Music Therapy in Stroke Rehabilitation vol. 7, (2013).
- [12] B.B. Johansson, Multisensory stimulation in stroke rehabilitation, *Front. Hum. Neurosci.* 6 (2012) 60.
- [13] P. Kirk, M. Grierson, R. Bodak, N. Ward, F. Brander, K. Kelly, N. Newman, L. Stewart, Motivating stroke rehabilitation through music: a feasibility study using digital musical instruments in the home, 34th Annual Chi Conference on Human Factors in Computing Systems, Chi (2016) 1781–1785 2016.
- [14] D.K. Zondervan, N. Friedman, E. Chang, X. Zhao, R. Augsburg, D.J. Reinkensmeyer, S.C. Cramer, Home-based hand rehabilitation after chronic stroke: randomized, controlled single-blind trial comparing the MusicGlove with a conventional exercise program, *J. Rehabil. Res. Dev.* 53 (2016) 457–472.
- [15] G. Lubrini, A. Martin-Montes, O. Diez-Ascaso, E. Diez-Tejedor, Brain disease, connectivity, plasticity and cognitive therapy: a neurological view of mental disorders, *Neurologia* 33 (2018) 187–191.
- [16] M.S. Kaplan, Plasticity after brain lesions: contemporary concepts, *Arch. Phys. Med. Rehabil.* 69 (1988) 984–991.
- [17] N. Friedman, V. Chan, A.N. Reinkensmeyer, A. Beroukhi, G.J. Zambrano, M. Bachman, D.J. Reinkensmeyer, Retraining and assessing hand movement after stroke using the MusicGlove: comparison with conventional hand therapy and isometric grip training, *J. Neuroeng. Rehabil.* 11 (2014).
- [18] P.H. Chang, S.H. Lee, G.M. Gu, S.H. Lee, S.H. Jin, S.S. Yeo, J.P. Seo, S.H. Jang, The cortical activation pattern by a rehabilitation robotic hand: a functional NIRS study, *Front. Hum. Neurosci.* 8 (2014) 49.
- [19] M.J. Kim, J.H. Hong, S.H. Jang, The cortical effect of clapping in the human brain: a functional MRI study, *NeuroRehabilitation* 28 (2011) 75–79.
- [20] S. Perrey, Non-invasive NIR spectroscopy of human brain function during exercise, *Methods* 45 (2008) 289–299.
- [21] L. Xu, B. Wang, G. Xu, W. Wang, Z. Liu, Z. Li, Functional connectivity analysis using fNIRS in healthy subjects during prolonged simulated driving, *Neurosci. Lett.* 640 (2017) 21–28.
- [22] L.G. Bu, C.C. Huo, Y.X. Qin, G.C. Xu, Y.H. Wang, Z.Y. Li, Effective connectivity in subjects with mild cognitive impairment as assessed using functional near-infrared spectroscopy, *Am. J. Phys. Med. Rehabil.* 98 (2019) 438–445.
- [23] C.A. Anderson, D.S. Lazard, D.E. Hartley, Plasticity in bilateral superior temporal cortex: effects of deafness and cochlear implantation on auditory and visual speech processing, *Hear. Res.* 343 (2017) 138–149.
- [24] P.H. Thakur, A.J. Bastian, S.S.J. Jo.N. Hsiao, Multidigit Movement Synergies of the Human Hand in an Unconstrained Haptic Exploration Task vol. 28, (2008), pp. 1271–1281.
- [25] L. Bu, D. Wang, C. Huo, G. Xu, Z. Li, J. Li, Effects of poor sleep quality on brain functional connectivity revealed by wavelet-based coherence analysis using NIRS methods in elderly subjects, *Neurosci. Lett.* 668 (2018) 108–114.
- [26] M. Uga, I. Dan, T. Sano, H. Dan, E. Watanabe, Optimizing the general linear model for functional near-infrared spectroscopy: an adaptive hemodynamic response function approach, *Neurophotonics* 1 (2014) 015004.
- [27] M.H. Chung, B. Martins, A. Privratsky, G.A. James, C.D. Kilts, K.A. Bush, Individual differences in rate of acquiring stable neural representations of tasks in fMRI, *PLoS One* 13 (2018) e0207352.
- [28] K. Kawabata Duncan, T. Tokuda, C. Sato, K. Tagai, I. Dan, Willingness-to-Pay-Associated right prefrontal activation during a single, real use of cosmetics as revealed by functional near-infrared spectroscopy, *Front. Hum. Neurosci.* 13 (2019) 16.
- [29] F. Irani, S.M. Platek, S. Bunce, A.C. Ruocco, D. Chute, Functional near infrared spectroscopy (fNIRS): an emerging neuroimaging technology with important applications for the study of brain disorders, *Clin. Neuropsychol.* 21 (2007) 9–37.
- [30] P.T. Fox, M.E. Raichle, M.A. Mintun, C. Dence, Nonoxidative glucose consumption during focal physiologic neural activity, *Science* 241 (1988) 462–464.
- [31] G. Lamp, P. Goodin, S. Palmer, E. Low, A. Barutchu, L.M. Carey, Activation of bilateral secondary somatosensory cortex with right hand touch stimulation: a meta-analysis of functional neuroimaging studies, *Front. Neurol.* 9 (2018) 1129.
- [32] L. Bunketorp-Kall, A. Lundgren-Nilsson, H. Samuelsson, T. Pekny, K. Blomve, M. Pekna, M. Pekny, C. Blomstrand, M. Nilsson, Long-term improvements after multimodal rehabilitation in late phase after stroke: a randomized controlled trial, *Stroke* 48 (2017) 1916–1924.
- [33] A.M. Tinga, J.M. Visser-Meily, M.J. van der Smagt, S. Van der Stigchel, R. van Ee, T.C. Nijboer, Multisensory stimulation to improve low- and higher-level sensory deficits after stroke: a systematic review, *Neuropsychol. Rev.* 26 (2016) 73–91.
- [34] C. Passamonti, I. Frissen, E. Ladavas, Visual recalibration of auditory spatial perception: two separate neural circuits for perceptual learning, *Eur. J. Neurosci.* 30 (2009) 1141–1150.
- [35] T. Bar-Shalita, Y. Granovsky, S. Parush, I. Weissman-Fogel, Sensory modulation disorder (SMD) and pain: a new perspective, *Front. Integr. Neurosci.* 13 (2019) 27.
- [36] B.E. Stein, Neural mechanisms for synthesizing sensory information and producing adaptive behaviors, *Exp. Brain Res.* 123 (1998) 124–135.
- [37] Y.K. Kim, E. Park, A. Lee, C.H. Im, Y.H. Kim, Changes in network connectivity during motor imagery and execution, *PLoS One* 13 (2018) e0190715.