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Acute Effect of Visually Induced Kinesthetic Illusion in Patients with Stroke: A Preliminary Report

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Abstract

A kinesthetic illusion induces a feeling as if an individual's own body is moving during sensory input, even though the body is actually in a resting state. In a previous study, we reported that a visually induced kinesthetic illusion (KiNVIS) increases corticospinal tract excitability that is associated with activity of the motor-association regions. The present study explored the acute effect of KiNVIS on motor function in five patients who had experienced stroke, as a preliminary study. Five Japanese patients with stroke, who had been otherwise healthy, participated in the present trial. During KiNVIS, a display was set over the forearm so that the position of the display would give the illusion that the patient's forearm was actually the same as that depicted in a movie. The movie showed a hand grasping and opening on the uninvolved side, and was repeatedly played for 15 min. Motor function was evaluated with the upper extremity section of the Fugl-Meyer Assessment (FMA-UE) as a primary outcome. Furthermore, we measured a performance of an appropriate motor task for each patient to detect change in motor function as a secondary outcome. In each patient, a positive effect on motor function was detected immediately after KiNVIS, and the appearance of reciprocal muscular control was observed in surface electromyography. There was no difference in the FMA-UE score between before and after the intervention; however, the score was slightly increased in two patients. Furthermore, upon comparison of the individual measurement results, each examination indicated positive changes in motor function. KiNVIS may have an acute positive effect in patients with stroke. The study provides, for the first time, evidence for the therapeutic potential of KiNVIS in stroke rehabilitation.

Keywords: Kinesthetic sense; Rehabilitation; Stroke

Introduction

We previously reported that a kinesthetic illusion, induced by a visual stimulus using a movie video (KiNVIS), produces vivid kinesthetic feeling in a healthy subject and in a patient with stroke, even though the body is actually in a resting condition [1-3]. The subjective kinesthesia felt in the first person during KiNVIS is generally vivid and, in our experience, stronger than that experienced during mirror therapy. We reported that, during KiNVIS, corticospinal tract excitability increases, as determined by transcranial magnetic stimulation (TMS) [1,2]. Furthermore, we showed, by functional magnetic resonance imaging, that a neural network is activated in the same brain regions during KiNVIS as is activated during actual movement execution [3]. Thus, the findings of our previous studies indicated that KiNVIS may induce a cerebral state similar to that induced by motor imagery, even though the kinesthetic perception during KiNVIS is "passively" induced. On the other hand, motor imagery describes the conscious and active psychological representation of movement. Motor imagery thus results in the activation of movement execution-related neural networks in healthy subjects [4-7].

A recently published consensus paper includes an approach to rehabilitation of stroke patients, i.e., adjustment of the abnormal inter-hemispheric inhibition [8] (for example, by repetitive transcranial magnetic stimulation, transcranial direct current stimulation, electrical neuromuscular stimulation, constraint-induced movement therapy involving intensive use of the affected hand), combined with motor relearning therapeutic exercises. Since KiNVIS increases corticospinal tract excitability and induces similar cerebral network activation as movement execution [3], we speculated that applying KiNVIS to a patient with stroke could induce a positive effect on sensory-motor function.

Additionally, mirror therapy and motor imagery are new tools that are currently favoured as therapeutic interventions for sensory-motor function recovery in patients with stroke. Several studies have indicated that mirror therapy has a positive effect on motor function in patients with stroke [9-12]. The neural substrate during mirror therapy and KiNVIS may overlap somewhat, since these two approaches include the psychological feeling of body ownership in the artificial body, in the mirror or the movie, and kinesthetic perception. However, there is a clear difference between these approaches in terms of the absence of actual movement of the patient's own body during KiNVIS, which may be reflected in some difference in brain activity. Moreover, although the efficacy of motor imagery on patients with stroke is limited by the patient's underlying pathophysiology [13] and is poorly reported [14], there is evidence that suggests that motor imagery provides additional benefits to conventional physiotherapy or occupational therapy [15].

Given this background, we speculated that KiNVIS may benefit patients with stroke. We had already confirmed that watching this type of movie could create an illusory perception of kinesthesia in a subject who had experienced a stroke more than 10 years previously; this patient also expressed a subjective feeling of desiring to move while watching the movie, as he perceived it as movement of his own hand. The aim of the present study was to assess the acute effect of KiNVIS on motor function in patients with stroke, as a preliminary study.

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Materials and Method

Five Japanese patients with stroke, who had been otherwise healthy, participated in the present trial. They had sensory and motor deficits after stroke. All of the patients were right-handed, and two patients had a stroke that affected their right-side (dominant), while the other two patients experienced a stroke that affected their left side. Their diagnoses were based on clinical evaluation and imaging (Table 1). The present study was approved by the local ethics committees (Sapporo Medical University and Asahikawa Rehabilitation Hospital).

Patient 1

The patient was a 51 year old man with damage to a wide area of the left putamen caused by a haemorrhagic stroke that had occurred 11 years previously. He had not had therapy for the involved right upper extremity (UE) since being discharged from the hospital 10 years earlier. This patient was independent in terms of activities of daily living and reported that he had not used his involved UE for functional activities. Voluntary movement was absent, with slight muscular contraction in the forearm and upper arm, and hand movement that was characterized by a flexor synergy pattern. The modified Ashworth scale score in the UE was 1. Tactile sensation was severely impaired throughout the UE.

Patient 2

The patient, a 23 year old man, was in the recovery phase. He had experienced infarction in the right posterior limb of the internal capsule, radiate crown, sensory area, and temporal lobe 27 weeks earlier. Movement of the left UE exhibited a flexor synergy pattern and hand movement was characterized by co-contraction of flexor and extensor muscles. Tactile sensation and sense of position were moderately impaired throughout the UE.

Patient 3

The patient, a 76 year old woman, was an in-patient in the recovery phase rehabilitation ward. She had experienced a left thalamus haemorrhage 17 weeks previously, but was medically stable. She participated in rehabilitative therapy for impairments in her right lower extremity, UE, and verbal ability, for 16 h per week. She needed assistance with most of the activities of daily living and her UE had not been in regular use since the stroke. Hand movement was characterized by a slight contraction of the flexor and extensor muscles. Tactile sensation was slightly impaired, and the sense of motion was moderately impaired throughout the UE.

Patient 4

The patient was an 85 year old man in the chronic phase after stroke. He had experienced infarction in the pons 30 weeks earlier. The left UE on the involved side was often used for functional activities. He could voluntarily flex the UE, but could not reach a computer mouse that was placed in front of him. Flexion and extension of the patient's fingers was partially possible. Tactile sensation was slightly impaired, and muscular tone was enhanced.

Patient 5

Patient 5, a 65 year old man, was an in-patient with a putamen infarction, and was unable to use his involved left UE voluntarily at all. Tactile sensation was slightly impaired, and muscular tone was slightly enhanced.

KiNVIS was applied for 15 min to test the acute effect on the participants' motor function. Patients were seated at a table with their forearm on the involved side supported on a soft cushion, and with their arm raised off the table to avoid any somatosensory input. During KiNVIS therapy, the patients remained fully relaxed and they were instructed not to move their hand. A liquid crystal display was set over the forearm and the position of the display was modulated precisely so that the forearm in the movie of the hand movement, which was pre-recorded prior to the therapeutic intervention, was adjusted to mirror the location of the patients' forearms from their individual viewpoint (Figure 1) [1,2]. The body size in the movie was adjusted to a size appropriate for the patient, so that body ownership could be induced by the movie, by making the patient feel as if their actual body was being displayed in real-time. The hand movement of the uninvolved side was recorded before the intervention. The movement task was chosen from among two kinds of movement (hand opening and closing, or wrist joint flexion and extension), based on the type of movement a physical therapist wanted the patient to learn. In a hand movement movie executed in the uninvolved side, the appointed movement was cyclically repeated for 30 s. After the movie length was edited, it was

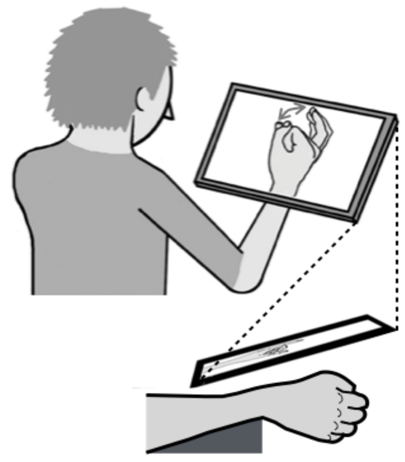

Figure 1: Schematic representation of kinesthetic illusion by visual stimulation. While the subject remained relaxed, kinesthetic illusion was induced by a visual stimulus using a movie of the hand movement.

	Age (years)	Sex	Diagnosis	Time after stroke	Lesion site	Paretic side	Handedness	Br. Stage (UE/Hand/LE)	MMSE	FMA (UE)	
										Pre	Post
Patient 1	51	Male	Hemorrhage	11 years	Putamen	Right	Right (corrected)	Ⅱ/Ⅱ/Ⅲ	30/30	2/66	5/66
Patient 2	23	Male	Infarction	27 weeks	Posterior limb of internal capsule, Radiate crown, Sensory area, Temporal lobe	Left	Right	Ⅴ/Ⅳ/Ⅳ	30/30	46/66	46/66
Patient 3	76	Female	Hemorrhage	17 weeks	Thalamus	Right	Right	Ⅳ/Ⅳ/Ⅳ	23/30	42/66	42/66
Patient 4	85	Male	Infarction	30 weeks	Pons	Left	Right	Ⅳ/Ⅳ/Ⅳ	29/30	35/66	35/66
Patient 5	65	Male	Hemorrhage	9 weeks	Putamen	Left	Right	Ⅱ/Ⅱ/Ⅳ	29/30	8/66	9/66

Table 1: Case descriptions of the five patients.

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flipped to mirror movement on the involved side, and was repeatedly projected for 15 min. In patient 1, KiNVIS was repeated once after motor examination for the same time period as the first intervention.

Before and immediately after the intervention, the motor functional state was evaluated using the upper extremity section of the Fugl-Meyer Assessment (FMA-UE) as a primary outcome in the present study. Furthermore, we assessed the performance of an appropriate motor task for each patient to detect changes in motor function, even though small, as secondary outcome. The task to be performed for monitoring the secondary outcome was chosen by a physiotherapist in charge of the patient's conventional physiotherapy in the hospital. The candidate tasks included simple movements of single joints (e.g. elbow flexion and extension), hand grasping and opening, and pinching for patients with severe motor paralysis. A peg-board task was used for patients with better motor function. Each patient repeated the set task three times and the average was calculated for each subject. Surface electromyography (sEMG), performed by means of a wireless system (TrignoTM wireless EMG, Delsys Inc., Natick, MA, USA), was recorded (sampling frequency; 4000 Hz, bandwidth 20 ± 5 Hz to 450 ± 50 Hz). Recordings were made in Patient 1 during elbow flexion and extension movement, from the biceps brachii and triceps brachii muscle, in Patient 2 during repeated pinch and release, from the flexer carpi radialis and extensor digitorum muscle, and in Patient 3 during maximal voluntary muscular contraction of hand grasp, from the flexer carpi radialis and extensor digitorum muscle. Hand grasp force was also measured in Patient 3. In Patient 2, we measured the time to transfer 20 pegs from a saucer to a peg-board, one by one, as rapidly as possible, to evaluate skilled performance. The peg-board (Manual Function Test SOT-5000, SAKAI Medical Co., Ltd., Tokyo, JAPAN) had 20 holes, which are 3 mm in diameter, and each peg was 2.5 mm in diameter. The range of motion of voluntary movement of the elbow joint (Patient 1), and hand movement (Patients 4 and 5) was measured using a video during each examination. In Patients 4 and 5, the angle of the starting position, maximum flexion, and extension angle of the metacarpophalangeal (MPj), proximal (PIPj), and distal (DIPj) interphalangeal joints of the paretic index finger were measured, both before and after the KiNVIS intervention. Flexion and extension angles of the movement arc (AMA) were obtained from those angles.

Results

Nobody complaint any unpleasant feeling during KiNVIS. The FMA-UE score measured before and after the intervention is shown in Table 1. In three (Patients 2, 3 and 4) of five patients, there was no change in the FMA-UE score between before and after the intervention; however, the score slightly increased in two patients.

In Patient 1, a marked change in voluntary movement was observed and the primary outcome showed improvement. The elbow joint flexion angle expanded to 56.1 degrees after KiNVIS, from 3.1 degrees before KiNVIS therapy. The sEMG values of the elbow flexor, during elbow flexion movement (Figure 2A), and the wrist flexor, during wrist flexion (Figure 2B), were increased after KiNVIS therapy. Furthermore, reciprocal contraction and relaxation of the wrist flexor and extensor muscles were observed after the 2nd round of KiNVIS therapy. In Patient 2, the FMA-UE score did not change immediately after the intervention. The time taken to complete the peg-board task, which was used as an indicator of his motor function, was shortened after KiNVIS therapy (Before: 2 min 53s, after: 2 min 32s). Additionally, the sEMG from the flexor and extensor muscles decreased after KiNVIS therapy, and the sEMG value of the extensors increased while releasing a peg (Figure 3). In Patient 3, the FMA-UE score did not change immediately after the intervention. The hand grasp force increased from 8.3 N before KiNVIS to 24.7 N after KiNVIS therapy (Figure 4A). The sEMG values of the extensors decreased and those of the flexors increased during the hand grasping task after KiNVIS therapy (Figure 4B). In the first three patients, reciprocal control of muscular activation was observed and voluntary control of movement was also found to be acutely improved after KiNVIS therapy. In Patients 4 and 5, the range of motion, which was measured during voluntary execution of hand grasping and

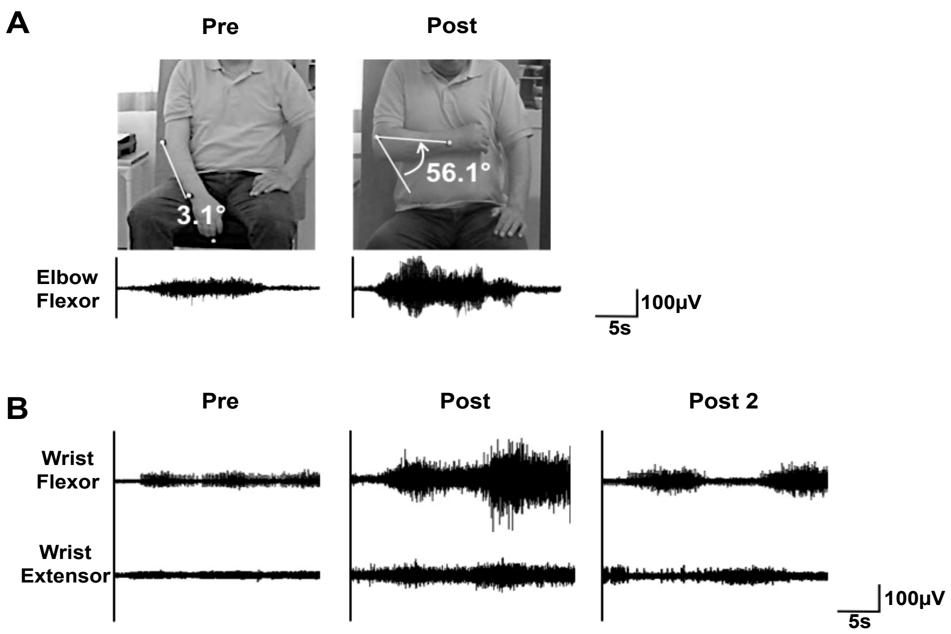
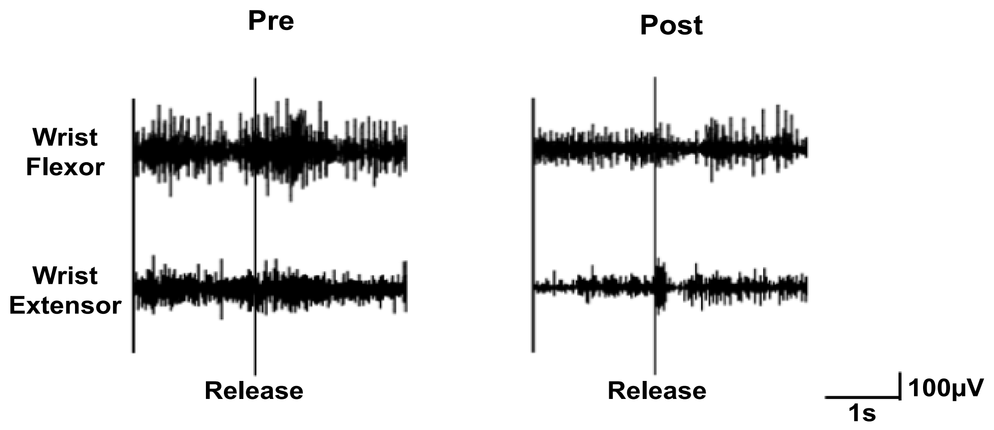


Figure 2: The range of motion and surface electromyography values in Patient 1. The elbow flexion angle and surface electromyography (sEMG) value of right biceps brachii during elbow flexion (A). sEMG value of right flexor carpi radialis and extensor carpi radialis during wrist flexion (B).



*Pre: before intervention; Post: after first intervention; Post 2: after second intervention

Figure 3: Surface electromyography value in Patient 2. sEMG value of left extensor digitorum and flexor carpi radialis during a peg-board task.

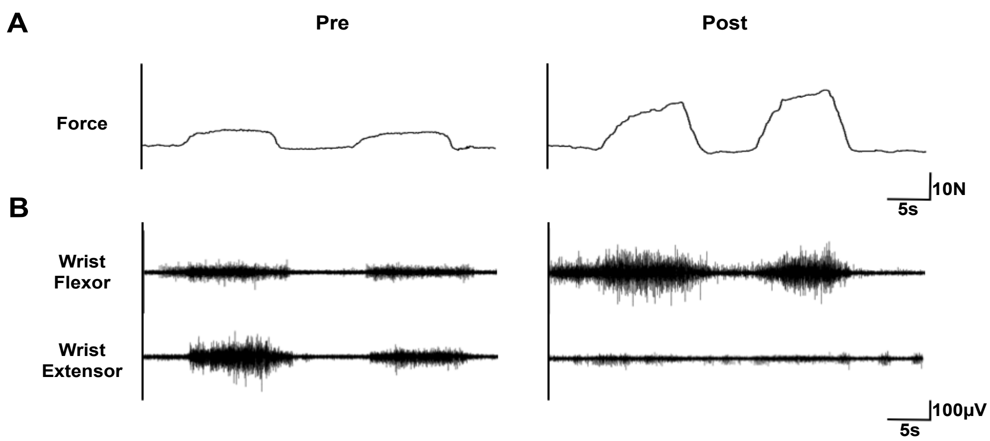


Figure 4: Surface electromyography value in Patient 3. Maximum force (A) and sEMG value of right digitorum flexors and extensor carpi radialis (B) during hand grasping.

		Flexion			Extension		
		MP	PIP	DIP	MP	PIP	DIP
Patient 4	Pre	31.7	54	33.9	31.4	68.7	39.5
	Post	35	69.4	47.6	37	66.3	47.6
Patient 5	Pre	0	0	0			
	Post	10.6	16.3	0			

Table 2: The range of motion during voluntary execution of hand grasping and opening in patients 4 and 5.

opening, were observed to increase (Table 2). The FMA-UE score did not change in Patient 4, but was slightly improved in Patient 5.

Discussion

As there has been no study to date in which KiNVIS has been applied as a therapeutic approach to patients with stroke, we considered it necessary to perform a preliminary study prior to performing a systematic prospective study to examine the therapeutic effect of this approach. We found that the effect of KiNVIS therapy on the five patients was not constant in terms of the primary outcome of the present study. This may suggest that KiNVIS did not have a clear acute effect that is measurable in terms of the FMA-UE score in the various patients who participated in the present study. However, importantly, we observed certain improvements in individual motor function, as determined by arbitrary functional examination, depending on the motor function of each patient. The sEMG data showed quantitative changes in muscular activation in Patient 1, and appearance of a form of reciprocal control of agonist-antagonist muscles in Patients 1, 2 and 3. The active range of motion in of a particular, relevant joint in the individual patients improved in Patients 1, 4, and 5. Generally, the results of comparisons of the individual measurements that were examined as secondary outcome before and after KiNVIS were positive. This suggests the possibility of using KiNVIS as a therapeutic approach for improving motor function in patients with stroke. Although the primary outcome was certainly not affected by KiNVIS therapy, improvement of motor functions in the individual forms the basis for improving the score used as the primary outcome, if it were sustained. Therefore, our results indicate that KiNVIS is sufficiently promising to warrant a well-organized prospective study.

The use of KiNVIS is consistent with a recently published consensus report on the optimal strategy for repairing motor function after stroke, which included an approach for improving abnormal inter-hemispheric inhibition [8]. Since KiNVIS affects corticospinal tract excitability and induces motor control-associated cerebral network activation [1-3], we speculated that KiNVIS could induce a positive effect on sensory-motor function in patients with stroke. In consideration based on the cerebral network activation during KiNVIS [3], the activation of the fronto-parietal neural network, which is associated with visuo-motor tasks [16-19] and the mirror neuron system [20], which is involved in activation of motor association areas (pre-motor cortex, supplementary motor cortex) during KiNVIS. This is plausible, as KiNVIS would induce activation of the motor association areas due to the input from the cerebral network through the superior longitudinal fasciculus [21]. This association network is different from that described in previous therapeutic interventions, for example, passive motion executed by means of robotic devices or neuromuscular electrical stimulation. Since the association neural networks in these previously described interventions mainly consist of projection fibers from the caudal organs, the frequent occurrence of stroke in the internal capsule, thalamus, and striatum would lead to functional disturbances of those neural networks.

From this viewpoint, KiNVIS may present a new therapeutic intervention for patients with stroke, as KiNVIS activates different networks from those typically affected and induces increases in the excitability of the motor association areas. Furthermore, KiNVIS does not contradict the hypothesis of abnormal inter-hemispheric inhibition [8]. If the effect noticed in the present study could be induced over the long term, using other interventions, such as conventional therapeutic exercise, and physical modalities, such as paired associated stimulation [22,23], therapeutic efficacy similar to brain stimulation may be achieved [24,25].

In addition to its effects on the pathophysiology, KiNVIS holds a practical advantage in that it is easier for patients to pay attention to the display in KiNVIS than it is during mirror therapy [26], since they do not need to move their contralateral hand. Paying attention to the mirror and moving the body simultaneously constitutes a dual task, which may be more difficult for elderly people than a single task [27,28].

Moreover, KiNVIS induces a particularly vivid kinesthetic feeling. The vividness of kinesthetic perception may be considered a measure of the effectiveness of KiNVIS. For instance, a patient commented on his subjective feeling that it was as if he remembered how to move his own hand, and felt able to recall the movement. It is uncertain how KiNVIS would contribute psychologically to the recall of movement in such patients; however, we speculate that the kinesthetic feeling created during KiNVIS enhances the ability to produce voluntary motor output.

The present study explored the acute effect of KiNVIS on motor function in five patients who had experienced stroke. KiNVIS therapy did not have a sufficient positive effect on the primary outcome of motor function; however, KiNVIS therapy acutely improved individual-specific motor functions in all five patients with stroke. The evidence presented here is weak, it is due to the low number of participants, the study is neither blind nor controlled, and there is a wide heterogeneity in the stroke features (age at onset; ischemic/haemorrhagic; time after the acute event; lesion and paretic side); however, these results indicate the need for a large-scale detailed study in the future. We consider that further well-organized prospective studies are warranted to explore the possibility of using KiNVIS as therapeutic intervention for improving sensory-motor functional impairments in patients with stroke.

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References

1. Kaneko F, Yasojima T, Kizuka T (2007) Kinesthetic illusory feeling induced by a finger movement movie effects on corticomotor excitability. Neuroscience 149: 976-984.
2. Aoyama T, Kaneko F, Hayami T, Shibata E (2012) The effects of kinesthetic illusory sensation induced by a visual stimulus on the corticomotor excitability of the leg muscles. Neurosci Lett 514: 106-109.
3. Kaneko F, Blanchard C, Lebar N, Nazarian B, Kavounoudias A, et al. (2015) Brain regions associated to a kinesthetic illusion evoked by watching a video of one's own moving hand. PLoS One 10: e0131970.
4. Roland PE, Larsen B, Lassen NA, Skinhøj E (1980) Supplementary motor area and other cortical areas in organization of voluntary movements in man. J Neurophysiol 43: 118-136.
5. Porro CA, Francescato MP, Cettolo V, Diamond ME, Baraldi P, et al. (1996) Primary motor and sensory cortex activation during motor performance and motor imagery: A functional magnetic resonance imaging study. J Neurosci 16: 7688-7698.
6. Roth M, Decety J, Raybaudi M, Massarelli R, Delon-Martin C, et al. (1996) Possible involvement of primary motor cortex in mentally simulated movement: A functional magnetic resonance imaging study. Neuroreport 7: 1280-1284.
7. Hanakawa T, Dimyan MA, Hallett M (2008) Motor planning, imagery and execution in the distributed motor network: A time-course study with functional MRI. Cereb Cortex 18: 2775-2788.
8. Hummel FC, Cohen LG (2006) Non-invasive brain stimulation: A new strategy to improve neurorehabilitation after stroke? Lancet Neurol 5: 708-712.
9. Yavuzer G, Selles R, Sezer N, Sütbeyaz S, Bussmann JB, et al. (2008) Mirror therapy improves hand function in subacute stroke: A randomized controlled trial. Arch Phys Med Rehabil 89: 393-398.
10. Michielsen ME, Selles RW, van der Geest JN, Eckhardt M, Yavuzer G, et al. (2011) Motor recovery and cortical reorganization after mirror therapy in chronic stroke patients: A phase II randomized controlled trial. Neurorehabil Neural Repair 25: 223-233.
11. Thieme H, Mehrholz J, Pohl M, Behrens J, Dohle C (2012) Mirror therapy for improving motor function after stroke. Cochrane Database of Systematic Reviews. 14: CD008449.
12. Invernizzi M, Negrini S, Carda S, Lanzotti L, Cisari C, et al. (2013) The value of adding mirror therapy for upper limb motor recovery of subacute stroke patients: A randomized controlled trial. Eur J Phys Rehabil Med 49: 311-317.
13. McInnes K, Friesen C, Boe S (2016) Specific brain lesions impair explicit motor imagery ability: A systematic review of the evidence. Arch Phys Med Rehabil 97: 478-489.
14. Harris JE, Hebert A (2015) Utilization of motor imagery in upper limb rehabilitation: A systematic scoping review. Clin Rehabil 29: 1092-1107.
15. Zimmermann-Schlatter A, Schuster C, Puhan MA, Siekierka E, Steurer J (2008) Efficacy of motor imagery in post-stroke rehabilitation: A systematic review. J Neuroeng Rehabil 5: 8.
16. Jeannerod M, Arbib MA, Rizzolatti G, Sakata H (1995) Grasping objects: The cortical mechanisms of visuomotor transformation. Trends Neurosci 18: 314-320.
17. Fagg AH, Arbib MA (1998) Modeling parietal-premotor interactions in primate control of grasping. Neural Netw 11: 1277-1303.
18. Frey SH, Vinton D, Norlund R, Grafton ST (2005) Cortical topography of human anterior intraparietal cortex active during visually guided grasping. Brain Res Cogn Brain Res 23: 397-405.
19. Cavanna AE, Trimble MR (2006) The precuneus: A review of its functional anatomy and behavioural correlates. Brain 129: 564-583.
20. Rizzolatti G, Craighero L (2004) The mirror-neuron system. Annu Rev Neurosci 27: 169-192.
21. Thiebaut de Schotten M1, Dell'Acqua F, Valabregue R, Catani M (2012) Monkey to human comparative anatomy of the frontal lobe association tracts. Cortex 48: 82-96.
22. Stefan K, Kunesch E, Cohen LG, Benecke R, Classen J (2000) Induction of plasticity in the human motor cortex by paired associative stimulation. Brain 123 Pt 3: 572-584.
23. Stefan K, Kunesch E, Benecke R, Cohen LG, Classen J (2002) Mechanisms of enhancement of human motor cortex excitability induced by interventional paired associative stimulation. J Physiol 543: 699-708.
24. Kim YH, Park JW, Ko MH, Jang SH, Lee PK (2004) Facilitative effect of high frequency sub-threshold repetitive transcranial magnetic stimulation on complex sequential motor learning in humans. Neurosci Lett 367: 181-185.

25. Hummel F, Celnik P, Giraux P, Floel A, Wu WH, et al. (2005) Effects of non-invasive cortical stimulation on skilled motor function in chronic stroke. Brain 128: 490-499.

26. Ramachandran VS, Rogers-Ramachandran D, Cobb S (1995) Touching the phantom limb. Nature 377: 489-490.

27. Zijlstra A, Ufkes T, Skelton DA, Lundin-Olsson L, Zijlstra W (2008) Do dual tasks have an added value over single tasks for balance assessment in fall prevention programs? A mini-review. Gerontology 54: 40-49.

28. Beurskens R, Bock O (2012) Age-related deficits of dual-task walking: A review. Neural Plast 2012: 131608.