NÖRO PSİKİYATRİ ARŞİVİ

Review

Arch Neuropsychiatry 2017; 54:358-363 • DOI: 10.5152/npa.2016.18056

Sensorimotor Integration During Motor Learning: Transcranial Magnetic Stimulation Studies

Zeliha MATUR[1], A. Emre ÖGE[2]

[1]Department of Neurology, İstanbul Bilim University School of Medicine, İstanbul, Turkey
[2]Department of Neurology, İstanbul University İstanbul School of Medicine, İstanbul, Turkey

ABSTRACT

The effect of sensory signals coming from skin and muscle afferents on the sensorimotor cortical networks is entitled as sensory-motor integration (SMI). SMI can be studied electrophysiologically by the motor cortex excitability changes in response to peripheral sensory stimulation. These changes include the periods of short afferent inhibition (SAI), afferent facilitation (AF), and late afferent inhibition (LAI). During the early period of motor skill acquisition, motor cortex excitability increases and changes occur in the area covered by the relevant zone of the motor cortex. In the late period, these give place to the morphological changes, such as synaptogenesis. SAI decreases during learning the motor skills, while LAI increases during motor activity. In this review, the role of SMI in the process of motor learning and transcranial magnetic stimulation techniques performed for studying SMI is summarized.

Keywords: Sensorimotor integration, transcranial magnetic stimulation, TMS, motor learning, motor skill learning

Cite this article as: Matur Z, Öge AE. Sensorimotor Integration During Motor Learning: Transcranial Magnetic Stimulation Studies. Arch Neuropsychiatry 2017; 54:358-363.

INTRODUCTION

How does becoming competent in the use of tools, playing an instrument, riding a bike, or becoming professional in a sports area, in other words, the "motor learning" process take place in the human brain? Are there factors negatively or positively affecting the motor learning process and if so, what are these? There are several studies that have been conducted or are being conducted on animals and humans with the purpose of seeking an answer to these questions. The findings from these studies show that the primary motor cortex (M1), basal ganglia, cerebellum, brainstem, and spinal cord are responsible for the learning of a motor skill in the human brain (1). The M1 is a superordinate control center that directly or indirectly (through interneurons) gives the necessary command to the anterior horn motor neurons for deliberate movement to occur.

Transcranial magnetic stimulation (TMS), which is a painless, non-invasive stimulation method, has been being widely used since 1985 when it was invented for investigating the functions of the central nervous system or for regulating or changing these functions with repetitive TMS (rTMS) protocols (2). Studies done with TMS have shown that different plastic changes occur in the M1 in both the early and the late periods during repetitive motor functions and the acquisition of a new motor skill (3,4,5,6,7,8,9).

Sensory and motor cortices are in communication and cooperation with each other in the regulation of movement; in other words, there is a sensory-motor integration (SMI). The M1 provides flexibility of movement by ensuring that the muscle groups that control the joints work in synergy and expertly uses the information coming from the sensory afferents while doing this (10). It has been known for a long time that signals coming from skin and muscle afferents affect the sensorimotor cortical networks in humans and other primates (11,12,13). Sensory afferents influence M1 either directly through the intracortical connections between the primary sensory cortex (S1) and M1 or through thalamocortical pathways that reach M1 (14,15).

Our knowledge on how SMI functions in the process of motor learning is based on the information obtained from animal experiments, the examination of patients with damage to the peripheral or central sensory pathways, and functional neuro-imaging studies. For example, the remarkable proper movement of the Caenorhabditis elegans, which is a nematode, with very few neurons in different and complex environments by using sensory signs, due to the very well-developed sensorimotor connections, has been demonstrated with studies (16). Both motor learning processes and the effect of proprioceptive and cutaneous afferent signals on corticospinal excitability can be studied using electrophysiological methods. Currently, it is known that SMI defects have also an underlying role in some movement disorders, such as dystonia (17). There is an accumulating evidence that SMI and motor learning can be changed through rTMS. Effects similar to long-term potentiation (LTP) and long-term depression (LTD) can be produced on cortical synaptic plasticity with different rTMS protocols (18,19,20). Nowadays, through the conditional proprioceptive feedback provided by the orthotic device called brain-robot-interface placed on the hand and arm during the motor imagery task, the completion of the sensorimotor cycle is ensured and additional benefits for regaining the motor

Correspondence Address: Zeliha Matur, İstanbul Bilim Üniversitesi Tıp Fakültesi, Nöroloji Anabilim Dalı, İstanbul, Türkiye
E-posta: zelihamatur@yahoo.co.uk

Received: 03.04.2016 **Accepted:** 15.05.2016

functions are aimed in patients with permanent and severe motor deficits following stroke (21).

Genetic variations have been shown to affect the motor learning process. For example, it was shown that the Val66Met (rs6265) "single nucleotide polymorphism" in the "brain-derived neuropathic factor" gene can affect the motor learning process in a negative way (22). Dopamine is an important neurotransmitter in motor skill learning and motor cortex plasticity. Variations in the five genes affecting the dopaminergic system (catechol O-methyltransferase [COMT]) that controls synaptic dopamine levels and those that encode the dopamine transfer protein and the D1, D2, and D3 dopamine receptors] have been reported to change motor learning (23).

This review summarizes the results of studies that seek answers to the questions: What are the plastic changes seen in the primary motor cortex during motor learning process?

How can SMI be assessed using electrophysiological methods? How does SMI affect the motor learning process?

WHAT ARE THE PLASTIC CHANGES SEEN IN THE PRIMARY MOTOR CORTEX DURING THE MOTOR LEARNING PROCESS?

The brain tissue has the capacity to develop functional and structural changes in response to experiences to which the body is exposed, which is expressed as "brain plasticity." Brain plasticity is a mechanism that is utilized in physiological processes, such as memory and the repair of damaged tissue regaining of impaired functions in pathological conditions. It has been demonstrated in rats and mice that during motor skill learning, reorganization and expansion occurs in the related motor cortex region where movement is represented in the primary motor cortex and an increased complexification and cortical synaptogenesis develop in the dendritic spines of the pyramidal neurons (24). Quick cortical plastic changes in relation to learning occur with the functional changes in the synapses. These include changes toward LTP and LTD in post-synaptic neurons or the surfacing of pre-existing connections; in other words, the awakening of silent synapses (18,19,20,25,26,27). However, time is needed for morphological changes, such as synaptogenesis, the reshaping of synapses and neurogenesis to emerge (28). Pharmacological studies have shown that motor cortical plastic changes due to use are related to the activation of N-methyl-D-aspartate receptors and gamma-aminobutyric acid (GABAergic) and that motor skill learning decreases the GABAergic inhibition in intracortical cycles (29). The GABAergic inhibitor system can be studied with paired-pulse TMS stimulation in humans (30).

Changes in the M1 in the motor learning process shown with TMS studies can be summarized as the motor threshold (MT), short interval intracortical inhibition (SICI), intracortical facilitation (ICF) changes, and display of changes in the site and size in the localization of the motor area related to the movement in question for motor mapping.

Motor threshold and motor-evoked potential (MEP) amplitude are parameters that show cortical excitability. Resting MT is the lowest stimulation intensity that creates an MEP response >0.05 mV in at least 5 out of 10 tries, and activity MT is the lowest stimulation intensity that creates an MEP response >0.1 mV in at least 5 out of 10 tries when the target muscle is in a state of slight contraction (31). The subject of M1 excitability changes in only the early period of motor learning is disputable. It has been shown in functional neuroimaging and TMS studies that during complex motor learning, the area where the movement is represented in the motor cortex expands and that the excitation threshold of this motor cortex area is decreased (3,32,33,34,35). Passive movements that do not require skill however did not lead to plastic changes or created very short-term minor changes (32,35,36). It has also been reported that repetitive movements that do not require skill led to a decrease lasting about 30 minutes in the modulation of synaptic transmission due to activity and M1 excitability (37,38,39,40). This decrease in excitability also occurs in the non-activated ipsilateral hemisphere with a slight delay (38). Thus, how are the cortical plastic changes that occur in people who continue motor exercises for a long time? It has been shown that in elite tennis players, the cortical map of the hand being used shifted and that the resting and active MTs decreased; no such change was found in normal people or social tennis players (9). This can be interpreted to mean that motor activities requiring skill lead to long-lasting motor plastic changes. Pascal Leone et al. (41) have shown that during the acquisition of a motor skill the related sensorimotor area expands and that this expansion begins to regress once the person has become professional. This is an indicator that a portion of quick motor cortical plastic changes give way to structural changes in the long term (28).

In paired-pulse TMS stimulation studies, the test stimuli are given at suprathreshold intensities, and the effect of a subthreshold conditioning stimuli that are given before the test stimuli with predetermined interstimulus intervals (ISI) on the motor responses evoked by the test stimuli are studied. Conditioning stimuli generally inhibit the motor responses if they are given with short ISIs (1-5 ms, short intracortical inhibition=SICI). This period is followed by an ICF with longer ISIs (8-25 ms) SICI and ICF are formed by different cortical interneuron groups (42). Short-term motor learning decreases SICI and may increase ICF or not affect it (43). It is different however in individuals who have a greatly developed control of the finger movements, for example musicians; while resting and active MTs are the same as controls, both SICI and ICF were found to be low (44). This may be indicative of extraordinary adaptation or maladaptation due to overuse.

HOW CAN SENSORY-MOTOR INTEGRATION BE ASSESSED USING ELECTROPHYSIOLOGICAL METHODS?

The recording of changes made on the motor response by sensory stimulation given a certain period before motor stimulation gives the electrophysiological information in the assessment of SMI. For this, TMS at suprathreshold intensity is applied to the motor cortex at certain ISIs by following peripheral nerve stimulation at suprathreshold submaximal intensity (Figure 1). Peripheral stimulation is performed through mixed or cutaneous nerves. The TMS intensity is usually at an intensity that forms a motor response at an amplitude of 1 mV in 5 out of 10 stimulations. A great majority of the studies have been performed on hand muscles. Different stimulation intensities, ISI, and the effect of register muscles were studied in detail. In studies conducted in the early period, TMS was performed with circular coils and then butterfly-shaped coils that can make more focal stimulation were used (45,46).

Motor-evoked potential amplitudes obtained with TMS change with peripheral stimulations given before it. This interaction consists of 3 stages depending on the period between peripheral nerve stimulation and TMS: short afferent inhibition (SAI), afferent facilitation (AF), and late afferent inhibition (LAI) (45,46,47,48,49,50,51) (Figure 2). While the differences shown by these interactions between people are significant, they are less in the examinations of the same person at different times. The degree of inhibition and facilitation are directly proportional to the intensity of nerve stimulation (52).

If the ISI between TMS and peripheral mixed-nerve stimulation is approximately close to the latency of the cortical N20 potential obtained in the somatosensory-evoked potential (SEP) examination (20-25 ms), it causes a reduction in the MEP amplitude. This condition is defined as EAI (47,49). EAI can develop by the afferent signals directly affecting the M1 neurons or indirectly through a sensory-motor short cycle. LAI is the second inhibition period and is shown for ISIs between 100 and 500 ms (48). Cortico-cortical or subcortical pathways probably play a role in their occurrence (50). Afferent signals also have a facilitating effect on the M1; this effect emerges with ISIs between 25 and 80 ms in the distal arm muscles (45,46) and with ISIs between 45 and 60 ms for leg muscles (45). AF has also been shown to continue while target muscles are in tonic contraction (51). Interestingly, AF occurs with the stimulation at the wrist level (mixed-nerve stimulation) of the median nerve but is not seen with the stimulation of skin branches (digital nerve) from the second finger. This may suggest that this facilitation occurs through thick afferent fibers stemming from muscle spindles (51,53). SMI shows topographic organization. This is because the greatest MEP changes are obtained by stimulation of the peripheral nerve innerving the register muscle (53,54).

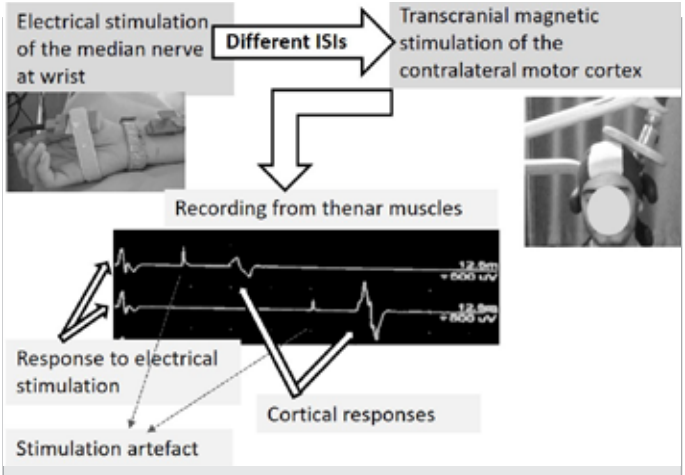

Figure 1. Sensory-motor integration study protocol

Short afferent inhibition afferent inhibition is believed to occur through acetylcholine (Ach) at the cortex level (55). Sailer et al. (50) showed that SAI can be changed with dopamine, and Di Lazzaro et al. (56) showed that it can be changed with gamma amino butyric acid A (GABAA) agonists. SAI interacts with neuronal cycles, such as SICI, driven by GABAergic interneurons (57,58) and long interval intracortical inhibition (59).

The magnitude of SAI can be changed. It increases with counting numbers (60) and decreases with finger movements or specific work (61,62). The rTMS also changes SAI. While low frequency rTMS applied to the S1 decreased SAI in patients with focal dystonia, it did not create any change in healthy controls (63). While 1 Hz rTMS applied to the M1 did not change SAI, it lowered MEP amplitudes in general (52). Intermittent theta burst stimulation (iTBS) on the M1 increased SAI in those with Parkinson's disease (64). While 30 Hz continuous TBS (cTBS) lowered MEP amplitudes when applied to the M1, it did not affect SAI; however, when it was applied to the S1 and S5 it increased MEP amplitudes and reduced SAI (65,66,67,68,69).

Late afferent inhibition increases during selective finger movements (62). Sensorial impairments that are not in the least lacking in Parkinson's patients are known to contribute to motor deficits. Sailer et al. (50) showed that SAI decreases in the hemisphere that is more affected under dopaminergic treatment in Parkinson's patients and it is similar to normal controls when dopaminergic treatment was ended, but showed that LAI decreased independently of treatment. They have stated that the difference between the SAI and LAI results stemmed from the difference between the underlying mechanisms of these two inhibition periods. While

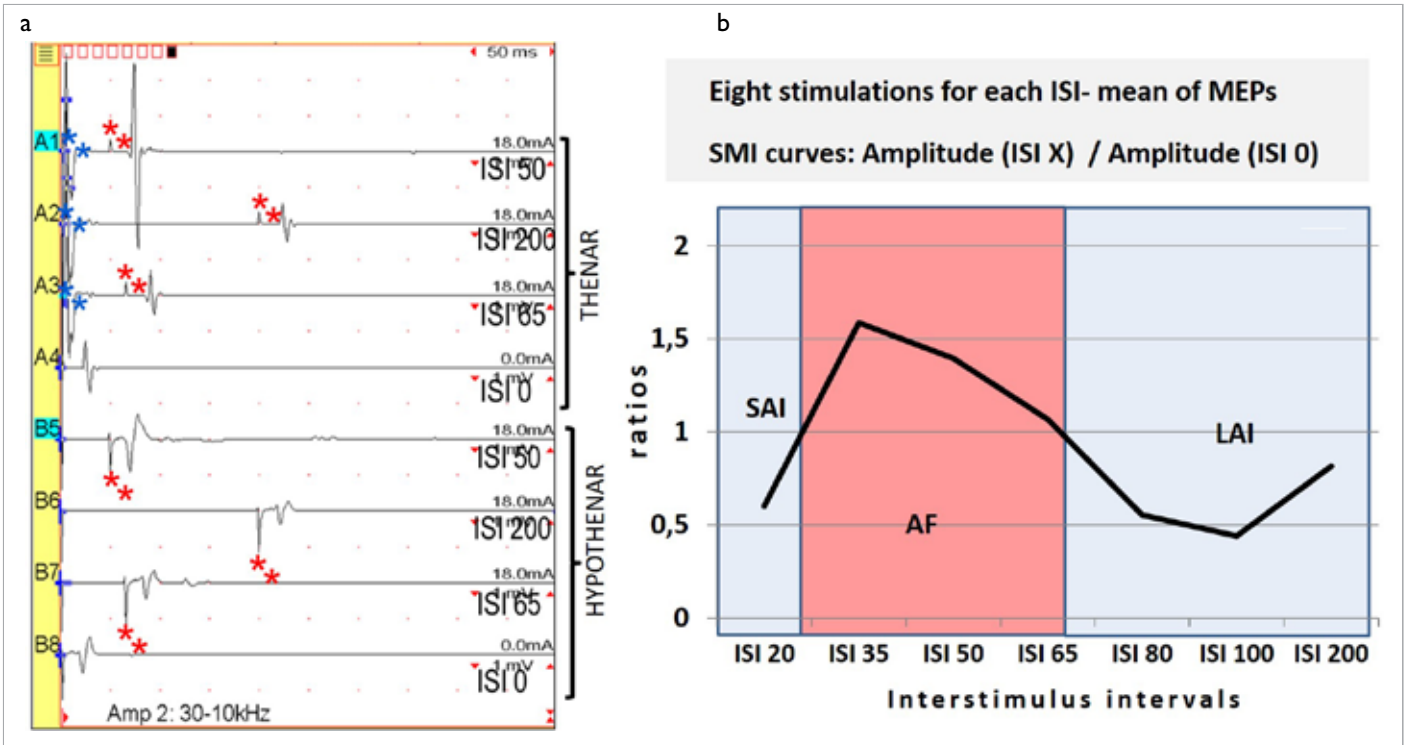

Figure 2. a, b. Effect of conditioning peripheral nerve stimulation on the size of motor evoked potentials evoked by transcranial magnetic stimulation of the motor cortex (TMS; test stimulation), which was applied after the conditioning stimuli with predetermined interstimulus intervals (a). The periods of sensory-motor integration: Short afferent inhibition (SAI), afferent facilitation (AF), and late afferent inhibition (LAI) (b)

SAI reflects the direct effect of the sensory stimulus on the motor cortex, LAI probably concerns the basal ganglia or cortical association areas.

HOW DOES SENSORY-MOTOR INTEGRATION EFFECT THE MOTOR LEARNING PROCESS?

Sensory feedback plays an important role in the learning of new motor skills. The effect of sensory input on motor learning is based on the information obtained from major animal experiments, the effects of sensory defects temporarily created in healthy people, and studies conducted with patients with peripheral sensory loss (70).

Peripheral sensory stimuli increase motor cortex excitability (71). While there is no reduction in strength in sensory neuropathies involving the thick myelinated fibers, motor skills are impaired (72). The somatosensory cortex is an important component in the acquisition of new motor skills. S1 probably increases M1 excitability with an LTP-like mechanism. When the S1 was cut off in macaque monkeys, it was found that the response characteristics of the cortical and spinal motor neurons had changed (73). When S1 ablation was performed in monkeys, it was seen that the acquisition of new motor skills was impaired in the opposite extremity but the previously learned skills continued without deterioration (74). One hertz rTMS applied to the S1 in healthy people impairs motor skill learning by causing the somatosensory feedback added to the internal model of movement organization or motor plan to be disrupted (70). A cTBS applied to the S1 decreases SEP amplitudes (75), while increases corticospinal excitability in the M1 (67,69). In the presence of post-central gyrus and intraparietal sulcus damage in patients who have had a stroke, the recovery of motor functions is definitely worse (76).

Carpal tunnel syndrome (CTS), which is a common entrapment neuropathy, can easily be studied as an appropriate disease model in investigating how a localized peripheral sensory impairment affects cortical SMI. Dropping objects and the impairment of manual skills requiring precision are seen very often in CTS. In a study we conducted, we found that in CTS patients who had and did not have a complaint of dropping objects, SMI started by the median and ulnar nerves topographically showed different shapes (77). We interpreted this to mean that brains with CTS responded by developing different strategies to the abnormal sensory information coming from the periphery. In another study, we investigated the change of SMI occurring during motor skill acquisition according to time and experience (78). We saw that basketball shots in sedentary subjects led to a decrease in SAI and an increase in AF and that this is more prominent in the early period; however, we found no such change in SMI in licensed basketball players. We interpreted the fact that there are no SMI changes in players who are still actively playing basketball to mean that these subjects are past the functional change stage seen in the early period during the process of motor skill acquisition.

CONCLUSION

The acquisition of motor skills leads to plastic changes in the motor cortex. Functional changes during the early period of learning mostly give way to permanent morphological changes in the late phase after motor memory has been formed. Peripheral sensory stimulation changes motor cortex excitability. Defects in sensory input impair motor skills. SMI can be studied electrophysiologically. While there is a decrease in SAI during the acquisition of a motor skill, LAI increases during motor activity.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Z.M.; Design - Z.M.; Supervision - A.E.Ö.; Resource - Z.M.; Materials -Z.M.; Data Collection and/or Processing - Z.M.; Analysis and/or Interpretation - Z.M.; Literature Search - Z.M., A.E.Ö.; Writing - Z.M.; Critical Reviews - A.E.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Shmuelof L, Krakauer JW. Are We Ready for a Natural History of Motor Learning? Neuron 2011; 72:469-476. [CrossRef]
2. Barker AT, Jalinous R, Freeston IL. Non-invasive stimulation of the human motor cortex. Lancet 1985; 2:1106-1107. [CrossRef]
3. Classen J, Liepert J, Wise SP, Hallett M, Cohen LG. Rapid plasticity of human cortical movement representation induced by practice. J Neurophysiol 1998; 79:1117-1123. [CrossRef]
4. Donoghue JP. Plasticity of adult sensorimotor representations. Curr Opin Neurobiol 1995; 5:749-754. [CrossRef]
5. Muellbacher W, Ziemann U, Boroojerdi B, Cohen L, Hallett M. Role of the human motor cortex in rapid motor learning. Exp Brain Res 2001;136:431-438. [CrossRef]
6. Sanes JN, Donoghue JP. Plasticity and primary motor cortex. Annu Rev Neurosci 2000; 23:393-415. [CrossRef]
7. Pascual-Leone A, Torres F. Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers. Brain 1993; 116:39-52. [CrossRef]
8. Pascual-Leone A, Wassermann EM, Sadato N, Hallett M. The role of reading activity on the modulation of motor cortical outputs to the reading hand in Braille readers. Ann Neurol 1995; 38:910-915. [CrossRef]
9. Pearce AJ, Thickbroom GW, Byrnes ML, Mastaglia FL. Functional reorganisation of the corticomotor projection to the hand in skilled racquet players. Exp Brain Res 2000; 130:238-243. [CrossRef]
10. Pruszynski JA, Kurtzer I, Nashed JY, Omrani M, Brouwer B, Scott SH. Primary motor cortex underlies multi-joint integration for fast feedback control. Nature 2011; 478:387-390. [CrossRef]
11. Marsden CD, Merton PA, Morton HB. Is the human stretch reflex cortical rather than spinal? Lancet 1973; 1:759-761. [CrossRef]
12. Rossini PM, Rossi S, Tecchio F, Pasqualetti P, Finazzi-Agrò A, Sabato A. Focal brain stimulation in healthy humans: motor maps changes following partial hand sensory deprivation. Neurosci Lett 1996; 214:191-195. [CrossRef]
13. Evarts, EV. Motor cortex reflexes associated with learned movement. Science 1973; 179:501-503. [CrossRef]
14. Chakrabarti S, Zhang M, Alloway KD. MI neuronal responses to peripheral whisker stimulation: relationship to neuronal activity in SI barrels and septa. J Neurophysiol 2008; 100:50-63. [CrossRef]
15. Rocco-Donovan M, Ramos RL, Giraldo S, Brumberg JC. Characteristics of synaptic connections between rodent primary somatosensory and motor cortices. Somatosens Mot Res 2011; 28:63-72. [CrossRef]
16. Samuel AD, Sengupta P. Sensorimotor integration: locating locomotion in neural circuits. Curr Biol 2005;15:R341-343. [CrossRef]
17. Abbruzzese G, Berardelli A. Sensorimotor integration in movement disorders. Mov. Disord 2003; 18:231-240. [CrossRef]
18. Ziemann U. LTP-like plasticity in human motor cortex. Suppl Clin Neurophysiol 2004; 57:702-707. [CrossRef]
19. Stefan K, Kunesch E, Cohen LG, Benecke R, Classen J. Induction of plasticity in the human motor cortex by paired associative stimulation. Brain 2000; 123:572-584. [CrossRef]
20. Jung SH, Shin JE, Jeong YS, Shin HI. Changes in motor cortical excitability induced by high-frequency repetitive transcranial magnetic stimulation of different stimulation durations. Clin Neurophysiol 2008; 119:71-79. [CrossRef]
21. Kraus D, Naros G, Bauer R, Leão MT, Ziemann U, Gharabaghi A. Brain-robot interface driven plasticity: Distributed modulation of corticospinal excitability. Neuroimage 2015; pii: S1053811915(15)00979-9.
22. Cirillo J, Hughes J, Ridding M, Thomas PQ, Semmler JG. Differential modulation of motor cortex excitability in BDNF Met allele carriers following experimentally induced and use-dependent plasticity. Eur J Neurosci 2012; 36: 2640-2649. [CrossRef]
23. Pearson-Fuhrhop KM, Minton B, Acevedo D, Shahbaba B, Cramer SC. Genetic variation in the human brain dopamine system influences motor learning and its modulation by L-Dopa. PLoS One 2013; 8:e61197. [CrossRef]
24. Diaz Heijtz R, Forssberg H. Translational studies exploring neuroplasticity associated with motor skill learning and the regulatory role of the dopamine system. Dev Med Child Neurol 2015; 57:10-14. [CrossRef]

25. Martin SJ, Grimwood PD, Morris RG. Synaptic plasticity and memory: an evaluation of the hypothesis. Annu Rev Neurosci 2000; 23:649-711. [CrossRef]
26. Jacobs KM, Donoghue JP. Reshaping the cortical motor map by unmasking latent intracortical connections. Science 1991; 251:944-947. [CrossRef]
27. Malinow R, Mainen ZF, Hayashi Y. LTP mechanisms: from silence to four-lane traffic. Curr Opin Neurobiol 2000; 10:352-357. [CrossRef]
28. Ljubisavljevic M. Transcranial magnetic stimulation and the motor learning-associated cortical plasticity. Exp Brain Res 2006; 173:215-222. [CrossRef]
29. Bütefisch CM, Davis BC, Wise SP, Sawaki L, Kopylev L, Classen J, Cohen LG. Mechanisms of use-dependent plasticity in the human motor cortex. Proc Natl Acad Sci USA 2000; 97:3661-3665. [CrossRef]
30. Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, Wroe S, Asselman P, Marsden CD. Corticocortical inhibition in human motor cortex. J Physiol 1993; 471:501-519. [CrossRef]
31. Rossini PM, Burke D, Chen R, Cohen LG, Daskalakis Z, Di Iorio R, Di Lazzaro V, Ferreri F, Fitzgerald PB, George MS, Hallett M, Lefaucheur JP, Langguth B, Matsumoto H, Miniussi C, Nitsche MA, Pascual-Leone A, Paulus W, Rossi S, Rothwell JC, Siebner HR, Ugawa Y, Walsh V, Ziemann U. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. Clin Neurophysiol 2015; 126:1071-1107. [CrossRef]
32. Pascual-Leone A, Nguyet D, Cohen LG, Brasil-Neto JP, Cammarota A, Hallett M. Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills. J Neurophysiol 1995; 74:1037-1045. [CrossRef]
33. Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E. Increased cortical representation of the fingers of the left hand in string players. Science 1995; 270:305-307. [CrossRef]
34. Karni A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerleider LG. Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Nature 1995; 377:155-158. [CrossRef]
35. Lotze M, Braun C, Birbaumer N, Anders S, Cohen LG. Motor learning elicited by voluntary drive. Brain 2003; 126:866-872. [CrossRef]
36. Tinazzi M, Farina S, Tamburin S, Facchini S, Fiaschi A, Restivo D, Berardelli A. Task-dependent modulation of excitatory and inhibitory functions within the human primary motor cortex. Exp Brain Res 2003; 150:222-229. [CrossRef]
37. Bonato C, Zanette G, Polo A, Bongiovanni G, Manganotti P, Tinazzi M, Teatini F, Fiaschi A. Cortical output modulation after rapid repetitive movements. Ital J Neurol Sci 1994; 15:489-494. [CrossRef]
38. Bonato C, Zanette G, Manganotti P, Tinazzi M, Bongiovanni G, Polo A, Fiaschi A. 'Direct' and 'crossed' modulation of human motor cortex excitability following exercise. Neurosci Lett 1996; 216:97-100. [CrossRef]
39. Bonato C, Zanette G, Fiaschi A, Rossini PM. Activity-dependent modulation of synaptic transmission in the intact human motor cortex revealed with transcranial magnetic stimulation. Cereb Cortex 2002; 12:1057-1062. [CrossRef]
40. Zanette G, Bonato C, Polo A, Tinazzi M, Manganotti P, Fiaschi A. Long-lasting depression of motor-evoked potentials to transcranial magnetic stimulation following exercise. Exp Brain Res 1995; 107:80-86. [CrossRef]
41. Pascual-Leone A, Grafman J, Hallett M. Modulation of cortical motor output maps during development of implicit and explicit knowledge. Science 1994; 263:1287-1289. [CrossRef]
42. Ziemann U, Rothwell JC, Ridding MC. Interaction between intracortical inhibition and facilitation in human motor cortex. J Physiol 1996; 496:873-881. [CrossRef]
43. Perez MA, Lungholt BK, Nyborg K, Nielsen JB. Motor skill training induces changes in the excitability of the leg cortical area in healthy humans. Exp Brain Res 2004; 159:197-205. [CrossRef]
44. Nordstrom MA, Butler SL. Reduced intracortical inhibition and facilitation of corticospinal neurons in musicians. Exp Brain Res 2002; 144:336-342. [CrossRef]
45. Deletis V, Schild JH, Beric A, Dimitrijevic MR. Facilitation of motor evoked potentials by somatosensory afferent stimulation. Electroencephalogr Clin Neurophysiol 1992; 85:302-310. [CrossRef]
46. Komori T, Watson BV, Brown WF. Influence of peripheral afferents on cortical and spinal motoneuron excitability. Muscle Nerve 1992; 15:48-51. [CrossRef]
47. Delwaide PJ, Olivier E. Conditioning transcranial cortical stimulation (TCCS) by exteroceptive stimulation in parkinsonian patients. In Streiffler MB, Korczyn AD, Melamed E, Youdim MBH. (Eds), Advances in Neurology: Parkinson's Disease; Anatomy, Pathology and Therapy. Raven Press, New York; 1990. pp.175-181.
48. Chen R, Corwell B, Hallett M. Modulation of motor cortex excitability by median nerve and digit stimulation. Exp Brain Res 1999; 129:77-86. [CrossRef]
49. Tokimura H, Di Lazzaro V, Tokimura Y, Oliviero A, Profice P, Insola A, et al. Short latency inhibition of human hand motor cortex by somatosensory input from the hand. J Physiol 2000; 523:503-513. [CrossRef]
50. Sailer A, Molnar GF, Paradiso G, Gunraj CA, Lang AE, Chen R. Short and long latency afferent inhibition in Parkinson's disease. Brain 2003; 126:1883-1894. [CrossRef]
51. Devanne H, Degardin A, Tyvaert L, Bocquillon P, Houdayer E, Manceaux A, Derambure P, Cassim F. Afferent-induced facilitation of primary motor cortex excitability in the region controlling hand muscles in humans. Eur J Neurosci 2009; 30:439-448. [CrossRef]
52. Fischer M, Orth M. Short-latency sensory afferent inhibition: conditioning stimulus intensity, recording site, and effects of 1 Hz repetitive TMS. Brain Stimul 2011; 4:202-209. [CrossRef]
53. Tamburin S, Manganotti P, Zanette G, Fiaschi A. Cutaneomotor integration in human hand motor areas: somatotopic effect and interaction of afferents. Exp Brain Res 2001; 141:232-241. [CrossRef]
54. Classen J, Steinfelder B, Liepert J, Stefan K, Celnik P, Cohen LG, Hess A, Kunesch E, Chen R, Benecke R, Hallett M. Cutaneomotor integration in humans is somatotopically organized at various levels of the nervous system and is task dependent. Exp Brain Res 2000; 130:48-59. [CrossRef]
55. Di Lazzaro V, Oliviero A, Profice P, Pennisi MA, Di Giovanni S, Zito G, Tonali P, Rothwell JC. Muscarinic receptor blockade has differential effects on the excitability of intracortical circuits in the human motor cortex. Exp Brain Res 2000;135:455-461. [CrossRef]
56. Di Lazzaro V, Oliviero A, Saturno E, Dileone M, Pilato F, Nardone R, Ranieri F, Musumeci G, Fiorilla T, Tonali P. Effects of lorazepam on short latency afferent inhibition and short latency intracortical inhibition in humans. J Physiol 2005; 564:661-668. [CrossRef]
57. Alle H, Heidegger T, Kriváneková L, Ziemann U. Interactions between short-interval intracortical inhibition and short-latency afferent inhibition in human motor cortex. J Physiol 2009; 587:5163-5176. [CrossRef]
58. Tsutsumi R, Shirota Y, Ohminami S, Terao Y, Ugawa Y, Hanajima R. Conditioning intensity-dependent interaction between short-latency interhemispheric inhibition and short-latency afferent inhibition. J Neurophysiol 2012; 108:1130-1137. [CrossRef]
59. Udupa K, Ni Z, Gunraj C, Chen R. Interactions between short latency afferent inhibition and long interval intracortical inhibition. Exp Brain Res 2009; 199:177-183. [CrossRef]
60. Kotb MA, Mima T, Ueki Y, Begum T, Khafagi AT, Fukuyama H, Nagamine T. Effect of spatial attention on human sensorimotor integration studied by transcranial magnetic stimulation. Clin Neurophysiol 2005;116:1195-1200. [CrossRef]
61. Asmussen MJ, Jacobs MF, Lee KGH, Zapallow CM, Nelson AJ. Short-latency afferent inhibition modulation during finger movement. PLoS One 2013; 8:e60496. [CrossRef]
62. Voller B, St Clair Gibson A, Lomarev M, Kanchana S, Dambrosia J, Dang N, Hallett M. Long-latency afferent inhibition during selective finger movement. J Neurophysiol 2005; 94:1115-1119. [CrossRef]
63. Bäumer T, Demiralay C, Hidding U, Bikmullina R, Helmich RC, Wunderlich S, Rothwell J, Liepert J, Siebner HR, Münchau A. Abnormal plasticity of the sensorimotor cortex to slow repetitive transcranial magnetic stimulation in patients with writer's cramp. Mov Disord 2007; 22:81-90. [CrossRef]
64. Zamir O, Gunraj C, Ni Z, Mazzella F, Chen R. Effects of theta burst stimulation on motor cortex excitability in Parkinson's disease. Clin Neurophysiol 2012; 123:815-821. [CrossRef]
65. Goldsworthy MR, Pitcher JB, Ridding MC. A comparison of two different continuous theta burst stimulation paradigms applied to the human primary motor cortex. Clin Neurophysiol 2012; 123:2256-2263. [CrossRef]

66. Jacobs MF, Zapallow CM, Tsang P, Lee KG, Asmussen MJ, Nelson AJ. Current direction specificity of continuous theta-burst stimulation in modulating human motor cortex excitability when applied to somatosensory cortex. Neuroreport 2012; 23:927-931. [CrossRef]
67. Jacobs MF, Tsang P, Lee KG, Asmussen MJ, Zapallow CM, Nelson AJ. 30 Hz theta-burst stimulation over primary somatosensory cortex modulates corticospinal output to the hand. Brain Stimul 2014; 7:269-274. [CrossRef]
68. Premji A, Rai N, Nelson A. Area 5 influences excitability within the primary motor cortex in humans. PLoS One 2011; 6:e20023. [CrossRef]
69. Tsang P, Jacobs MF, Lee KGH, Asmussen MJ, Zapallow, CM, Nelson AJ. Continuous theta-burst stimulation over primary somatosensory cortex modulates short-latency afferent inhibition. Clin Neurophysiol 2014; 125:2253-2259. [CrossRef]
70. Vidoni ED, Acerra NE, Dao E, Meehan SK, Boyd LA. Role of the primary somatosensory cortex in motor learning: An rTMS study. Neurobiol Learn Mem 2010; 93:532-539. [CrossRef]
71. Hamdy S, Rothwell JC, Aziz Q, Singh KD, Thompson DG. Long-term reorganization of human motor cortex driven by short-term sensory stimulation. Nat Neurosci 1998; 1:64-68. [CrossRef]
72. Sanes JN, Mauritz KH, Evarts EV, Dalakas MC, Chu A. Motor deficits in patients with large-fiber sensory neuropathy. Proc Natl Acad Sci USA 1984; 81:979-982. [CrossRef]
73. Brinkman J, Colebatch JG, Porter R, York DH. Responses of precentral cells during cooling of postcentral cortex in conscious monkeys. J Physiol (Lond) 1985; 368:611-625. [CrossRef]
74. Pavlides C, Miyashita E, Asanuma H. Projection from the sensory to the motor cortex is important in learning motor skills in the monkey. J Neurophysiol 1993; 70:733-741. [CrossRef]
75. Ishikawa S, Matsunaga K, Nakanishi R, Kawahira K, Murayama N, Tsuji S, Huang YZ, Rothwell JC. Effect of theta burst stimulation over the human sensorimotor cortex on motor and somatosensory evoked potentials. Clin Neurophysiol 2007; 118:1033-1043. [CrossRef]
76. Abela E, Missimer J, Wiest R, Federspiel A, Hess C, Sturzenegger M, Weder B. Lesions to primary sensory and posterior parietal cortices impair recovery from hand paresis after stroke. PLoS One 2012; 7:e31275. [CrossRef]
77. Dörtcan N, Matur Z, Imisci S, Suner M, Taskiran E, Acar Z, Sozer-Topcular N, Oge AE. Dropping Objects in Carpal Tunnel Syndrome: Clinical Characteristics and Sensory-Motor Integration. 30th International Congress of Clinical Neurophysiology (ICCN), 20-23 Mart 2014, Berlin, Germany Abstracts, p.991.
78. Acar Z, Matur Z, Senturk G, Imısci S, Suner M, Kurt G, Oge AE. Effects of basketball shooting exerciıses on sensory-motor integration in normal controls and basketball players. 30th International Congress of Clinical Neurophysiology (ICCN), 20-23 Mart 2014, Berlin, Germany. Abstracts, p.1385.