# Cortical Plasticity in Patients with Incomplete Cervical Spinal Cord Injury; Effect of Massed Practice and Somatosensory Stimulation

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**Abstract:** Using transcranial magnetic stimulation (TMS) has shown that massed practice (MP) and somatosensory stimulation (SS) produce use-dependent cortical reorganization and can induce changes in the excitability of the cortical projections. **Aim of work:** was to compare between MP, MP with SS, and conventional rehabilitation techniques on cortical plasticity in patients with incomplete cervical spinal cord injury (SCI). **Patients and methods:** This prospective study included 25 patients with incomplete cervical SCI divided randomly into 3 groups: Group (I): received MP therapy and conventional rehabilitation (N=10). Group (II): received MP therapy, SS and conventional rehabilitation (N=10). Group (III): received conventional rehabilitation (N=5). TMS was performed to assess: Motor threshold (MT), peak-to-peak amplitude and latency. After 3 weeks of rehabilitation we compared pre and post TMS parameters in each group and the change in these parameters between the three groups. **Results:** There was a statistically significant decrease in motor threshold in groups I and group II ($P<0.05$) post-rehabilitation, while there was no statistically significant difference in amplitude or latency ($P>0.05$). There was no statistically significant difference post-rehabilitation as regards MT, amplitude and latency ingroup (III) ($P>0.05$). On comparing between the 3 groups: Groups (I) and (II) showed a greater decrease in the MT and a greater increase in the amplitude of MEP than group (III) but the difference was of no statistical significance ($P>0.05$). **Thus,** the combination of MP and SS results in changes in cortical excitability in patients with SCI manifested in the MT needed to elicit the MEP's.

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**Key words:** Cervical spinal cord injury, cortical plasticity, massed practice, somatosensory stimulation.

## 1. Introduction:

Incomplete cervical spinal cord injury (SCI) is currently the most common form of SCI (34.3% of all cases). Because approximately 61% of people with cervical SCI have functionally incomplete injuries, varying degrees of arm and hand function may be possible regardless of the level of the lesion Recovery of function after SCI largely depends on the preservation of some anatomic connections, and may also depend on the physiologic reorganization of the brain and spinal cord **(1)**.

There is evidence that massed practice (MP), of which constraint induced therapy (CIMT) is one form, promotes cortical reorganization. Using neuroimaging techniques and trans cranial magnetic stimulation (TMS) has shown that MP training produces an extensive use-dependent cortical reorganization **(2).**

Prolonged, repetitive peripheral nerve stimulation can induce changes in the excitability of the cortical projections of hand muscles, increase pinch strength and improve functional performance**(3).**

Afferent information may change cortical representations and/or improve motor performance in people with SCI, just as it does in normal people and people with stroke. A possible underlying mechanism is that the somatosensory cortex has an important role in cortical reorganization after injury. Cortical reorganization can be facilitated through training movements and /or electric stimulation techniques**(4).**

**Aim of the work:**

The aim of this work was to compare between the effect of MP, MP with SS, andconventional rehabilitation techniques on cortical plasticity in patients with incomplete cervical SCI.

## 2. Patients and Methods:

This prospective study included 25 patients with incomplete cervical SCI; according to American

Spinal Cord Injury Association Impairment Scale (ASIA) **(5)** after taking an informed consent. Patients were selected from Ain Shams University Hospitals and Armed Forces Rehabilitation Center. The local ethical committee approved this study.

**Inclusion Criteria:**

1. Patients between 16 and 60 years of age.
2. Duration of illness at least 6 months.
3. Patients demonstrated at least trace evidence of voluntary thumb movement (i.e. twitch).
4. Patients diagnosed with spastic paresis (manifested as spasms, clonus, or hyperreflexia) due to neurologically incomplete SCI.
5. Level of injury from C5 to C7.
6. Patients classified according to ASIA scale to either grade C or D.
7. No serious uncontrolled medical complication.

**Exclusion Criteria**

1. Patients with history of epilepsy as TMS at high stimulation intensities can induce seizures.
2. Patients with metallic devices such as aneurysm clips, cardiac pacemakers or metallic cervical cage or plate and screw to prevent the interference with the magnetic flux.
3. Patients with traumatic brain or brain stem injury.
4. Patients who could not cooperate due to dementia or psychosis.
5. Patients with skin diseases or burns at site of application that would prevent using recording electrodes.
6. Patients with upper extremity injury or conditions that limit the use of the upper limb before the SCI.
7. Patients with severe spasticity as defined as a score ≥ 3 on the Modified Ashworth Spasticity Scale.

All patients underwent the following:

I. Full medical history taking with special attention to handedness, and neurological symptoms.

II. Thorough clinical examination

Neurological examination including:

**a) Motor examination:**

***Muscle power*** using the ASIA motor index score which uses standard manual muscle testing on a six-grade scale (Brunnstrom and Dennen, 1940**) (6).** Numerically, the total possible upper extremity motor score (UEMS) obtained from the bilateral summation of muscle grades is 50 points.

***Deep tendon reflexes*** were rated according to Bates **(7)** from 0 to 4. ***Tone*** was rated according to Modified Ashworth Scale (Bohannon and Smith, 1987) **(8)** with grades from 0 to 5.

**b) Sensory examination**

The sensory system was examined for light touch and pin prick sensation. The sensation was tested for each sensory dermatome and graded on a three point scale from 0 to2 according to the standards of the ASIA **(5)**. The maximum sensory scores for the upper extremity (C2-T1) according to the summation of the sensory grades were 16 for the pinprick and 16 for the light touch.

**Neurological level:**

The overall neurologic level of injury was determined as the most caudal level at which both motor and sensory modalities are intact.

**c) PR examination**

Voluntary motor control of the external sphincter on digital examination and sensation around the anus were examined to assess the completeness of injury **(9).**

**d) ASIA Impairment Scale** of spinal cord injuries ranged from class A to class E according to ASIA standards **(5).**

III. **Transcranial Magnetic Stimulation (TMS):**

Motor evoked potentials (MEP's) from the thenar muscles were elicited using DANTEC Magnetic Stimulator MagLite Denmark MC-B70 machine.

The following parameters were measured:

i) Motor threshold (**MT**): The lowest stimulus intensity evoking MEP's > 50 µv amplitude **(10).**

ii) Peak to peak amplitude.

iii) Latency: time from the application of the stimulus till the start of the wave.

**Patients were divided into 3 groups**

**Group I**

Ten patients received MP training directed to the upper extremity having the lower motor score. The patients received this training program 5 times per week for 3 weeks, 2 hours per session **(11).**

MP focused on continuous repetition of tasks in each of 5 categories:

***a)*** **Gross upper extremity movement:** dart throw, baseball, ball -bounce, and paddle ball.

**a) Grip:** Coke can to mouth, squeezing toothpaste, slice play dough with plastic knife, cutting paper, fold towel. shapingplay dough, place in a jar.scoop sand and pour.

**b) Grip with rotation:** doorknob, lids on jars, flipping cards, screwing in a light bulb, pitcher pour into cup.

**c) Pinch:** writing circles and crosses, putting small objects into jar, pegboard, coins in change purse, connect 4, bubble wrap, buttons, find small objects in lentils.

**d) Pinch with rotation:** flipping cards, key in lock, lace-up, beads on string, screw and screwdriver, nuts and bolts, open nail polish jar.

The order of the categories was chosen randomly, the patients repeatedly performed the tasks within each category for 25 minutes before moving on to the next category. Total training time was 2 hours per session. Patient repeatedly performed 1 task at a time until fatigued. A 2-3 minutes break was allowed before the start of a new task within the same category.

When a task gradually became easier, we increased the difficulty. This was done to ensure that the tasks were sufficiently challenging because evidence suggests that tasks should be sufficiently challenging to induce cortical reorganization **(12)**.

**Group II**

Ten patients received MP training as in the first group in addition to SS directed to the upper extremity having the lower motor score.

SS was done for the median nerve at the level of the wrist for 2 hours. The apparatus used was the (Zimmer Elektromedizin Galva 5).

Patient received trains of electrical stimulation delivered at 1 Hz, each train consisted of 5 single pulses at 1 ms duration delivered at 10 Hz with stimulus intensity just below that which evoked an observable twitch in any of the muscles innervated by the median nerve. This type of stimulation preferentially activates large cutaneous and proprioceptive sensory fibers **(11).**

The optimal position for stimulating the median nerve at the wrist: electrodes placed at the site that elicited in the thenar muscles the maximal motor response to stimulation (anode at the wrist and cathode 2 cm proximal to it).

**Group III**

Five patients with incomplete cervical SCI as control received conventional rehabilitation program.

Patients in groups I and II received the conventional rehabilitation program besides MP with or without SS.

After 3 weeks of rehabilitation we compared the pre and post TMS parameters in each group and compared the change in these parameters between the three groups.

**Statistical analysis**

This was done using SPSS 10 for Windows (Statistical Package for the Social Sciences) to obtain:

1- Descriptive statistics:

i) Mean
ii) Standard deviation
iii) Range (min-max) for numerical data
iv) Number and % (for non-numerical data)

**2. Analytical statistics:**

i) Paired sample Student's "t" test was used to test the difference between pre and post values of some parameters (for continuous variables).

ii) Independent sample Student's "t" test was used to test the difference between two groups (for continuous variables).

iii) Chi-square test to compare between groups regarding non-numerical variables.

iv) Correlation (Pearson correlation coefficient =r) assessing strength and direction of the linear relationship between two variables.

v) One-way ANOVA test (F) was used to test difference between more than two means.

- *p*-value: level of significance:
- *P*> 0.05: Nonsignificant (NS).
- *P*< 0.05: Significant (S).
- *P*< 0.001: Highly significant (HS).

**3. Results:**

This study was carried on 25 patients with traumatic incomplete cervical SCI. Patients were selected from A in Shams University Hospitals and Armed Forces Rehabilitation Center. Patients received different rehabilitation modalities for 3 weeks.

**Patients were divided randomly into 3 groups according to the treatment modality used:**

Group (I): Patients in this group received MP therapy and conventional rehabilitation (N=10).

Group (II): Patients in this group received MP therapy, SS and conventional rehabilitation (N=10).

Group (III): Patients in this group received the conventional rehabilitation program (N=5).

**Descriptive data**

There was no statistically significant difference between the 3 groups (*p*>0.05) as regards the age, sex,handedness, disease duration, ASIA scale or level of injury as shown in tables**(1&2&3).**

**Comparison between pre and post-treatment values**

The motor score for both upper extremities was measured in all the patients. The rehabilitation program was directed to the upper extremity with the lower motor score.

After 3 weeks of rehabilitation we compared the pre and post TMS parameters in each group.

On comparing the pre and post treatment TMS measures in group (I), there was a statistically significant decrease in MT (*P*<0.05), while there was no statistically significant difference in amplitude or latency (*P*>0.05) as shown in table **(4)**.

Table (1): Comparison between the 3 groups as regards the age and disease duration

| | Groups (N) | Range (years) | Mean ± SD | f | *P*-value | Sig |
|---|---|---|---|---|---|---|
| Age (years) | Group I (10) | 25 – 45 | 33.2± 6.14 | 1.05 | 0.367 | NS |
| | Group II (10) | 24 - 60 | 38.7± 12.09 | | | |
| | Group III (5) | 25 - 41 | 33.4 ± 7.09 | | | |
| Duration of illness (month) | Group I | 8 – 72 | 21.8 ± 19.07 | 0.159 | 0.854 | NS |
| | Group II | 6 - 84 | 24.1 ±22.07 | | | |
| | Group III | 7 - 36 | 18 ± 12.19 | | | |

***N:** number of patients, **Sig:** Significance, **NS:**Non significant.*

*Table (2): Comparison between the 3 groups as regards the sex and handedness.*

| | | N | % | $\chi^2$ | P-value | Sig |
|---|---|---|---|---|---|---|
| **Sex** | **Group I** | | | 1.050 | 0.367 | NS |
| | Males | 8 | 80% | | | |
| | Females | 2 | 20% | | | |
| | **Group II** | | | | | |
| | Males | 8 | 80% | | | |
| | Females | 2 | 20% | | | |
| | **Group III** | | | | | |
| | Males | 3 | 60% | | | |
| | Females | 2 | 40% | | | |
| **Handedness** | **Group I** | | | 0.446 | 0.8 | NS |
| | Rt | 9 | 90% | | | |
| | Lt | 1 | 10% | | | |
| | **Group II** | | | | | |
| | Rt | 8 | 80% | | | |
| | Lt | 2 | 20% | | | |
| | **Group III** | | | | | |
| | Rt | 4 | 80% | | | |
| | Lt | 1 | 20% | | | |

Table (3): Comparison between the 3 groups as regards ASIA scale and level of injury.

| | | Number | % | $\chi^2$ | *P*-value | Sig |
|---|---|---|---|---|---|---|
| **ASIA** | **Group I** | | | 1.25 | 0.535 | NS |
| | C | 4 | 40% | | | |
| | D | 6 | 60% | | | |
| | **Group II** | | | | | |
| | C | 3 | 30% | | | |
| | D | 7 | 70% | | | |
| | **Group III** | | | | | |
| | C | 2 | 40% | | | |
| | D | 3 | 60% | | | |
| **Level** | **Group I** | | | 0.417 | 0.981 | NS |
| | C5 | 5 | 50% | | | |
| | C6 | 4 | 40% | | | |
| | C7 | 1 | 10% | | | |

Table (4): Comparison between pre and post treatment TMS measures in group (I).

| | Mean | ± | SD | Mean | ± | SD | t | *P*-value | Sig |
|---|---|---|---|---|---|---|---|---|---|
| MT (%MSO) | 91 | ± | 8.756 | 84 | ± | 13.499 | 3.28 | 0.01 | S |
| Amplitude (µV) | 158.571 | ± | 82.144 | 186.857 | ± | 98.839 | 1.383 | 0.216 | NS |
| Latency (msec) | 48.257 | ± | 14.282 | 44.071 | ± | 12.532 | 1.615 | 0.075 | NS |

**MSO:** Maximum stimulation output, **µV:** Microvolt, **msec**: Milliseconds, **Sig:** Significance, **NS:** Non significant, **S:** Significant

Comparison between pre and post treatment TMS measures in group (II) revealed, a statistically significant decrease in the MT (*P*<0.05), while there was no statistically significant difference as regards amplitude and latency (*P*>0.05) as shown in table **(5)**.

Table (5): Comparison between pre and post treatment TMS measures in group (II).

| | Mean ± SD | Mean ± SD | t | *P*-value | Sig |
|---|---|---|---|---|---|
| MT (%MO) | 88 ± 7.89 | 80 ± 12.47 | 4 | 0.003 | S |
| Amplitude (µV) | 124.25 ± 67.64 | 151.75 ± 72.84 | 1.701 | 0.131 | NS |
| Latency (msec) | 42.375 ± 14.56 | 37.988 ± 6.84 | 1.408 | 0.202 | NS |

There was no statistically significant difference between pre and post rehabilitation as regards MT, amplitude and latency in group (III) (*P*>0.05) as shown in table **(6).**

On comparing between the 3 groups together there was no significant difference between them regarding the MT, amplitude and latency (p>0.05).

Group I and II showed a greater decrease in the MT than group III but the difference was not of statistical significance (*P*>0.05).

Also groups (I) and (II) showed an increase in the amplitude of the MEP's after the treatment but the difference was not of statistical significance (*P*>0.05) as shown in table **(7).**

Table (6): Comparison between pre and post treatment TMS measures in group (III).

| | Mean ± SD | Mean ± SD | t | P-value | Sig |
|---|---|---|---|---|---|
| MT(%MSO) | 88 ± 13.038 | 86 ± 13.416 | 1 | 0.374 | NS |
| Amplitude (µV) | 152.5 ± 58.524 | 146 ± 52.889 | 1.857 | 0.16 | NS |
| Latency (msec) | 45.25 ± 8.273 | 44.825 ± 8.226 | 0.855 | 0.456 | NS |

Table (7): Comparison between the 3 groups as regards the TMS parameters.

| | | Group I Mean ± SD | Group II Mean ± SD | Group III Mean ± SD | F | p | Sig |
|---|---|---|---|---|---|---|---|
| MT (MSO) | Pre | 91±8.76 | 88±7.888 | 88±13.038 | 0.308 | 0.738 | NS |
| | Post | 84±13.5 | 80±12.472 | 86±13.416 | 0.421 | 0.661 | NS |
| | Change | -7±6.75 | -8±6.325 | -2±4.472 | 1.631 | 0.219 | NS |
| Amplitude (µV) | Pre | 158.57±82.14 | 124.25±67.641 | 152.5±58.52 | 0.471 | 0.633 | NS |
| | Post | 174.13±98.34 | 147.111±69.542 | 146±52.89 | 0.291 | 0.751 | NS |
| | Change | 28.29±54.1 | 27.5±28.799 | -6.5±7 | 1.27 | 0.308 | NS |
| Latency (msec) | Pre | 48.26±14.28 | 42.375±14.559 | 45.25±8.273 | 0.355 | 0.707 | NS |
| | Post | 44.13±11.60 | 42.389±14.672 | 44.825±8.226 | 0.067 | 0.936 | NS |
| | Change | -4.186±4.4 | -4.388±8.813 | -0.425±0.995 | 0.572 | 0.575 | NS |

## 4. Discussion:

Persons with cervical spinal cord injury believe that increasing upper limb function will improve their quality of life. Various lines of evidence demonstrate that persons with incomplete quadripareisis have the potential for improvements in both neural plasticity and function of the arms and hands. Therefore treatment to improve UL function should focus on improving motor control, not just compensation for the paralysis and sensory loss that follows a spinal cord injury**(13).**

It has been suggested that the recovery of upper-extremity function following a hemi-section of the cervical spinal cord in macaques is dependent on the ability to optimally use the limited information that is being transmitted via spared corticospinal connections. Investigators have concluded that it is the reduced rate of transmission of relevant information from the motor cortex to the spinal cord that limits performance. MP may maximize the effectiveness of corticospinal drive onto spinal motor neurons**(14).**

Therefore, afferent input in the form of repeated training movements and /or electric stimulation techniques may contribute to cortical reorganization and, ultimately, to functional recovery via increased communication between the cortex and the cervical spinal cord in SCI subjects**(15)**.

The purpose of this study was to compare between the effects of participation in a 3 weeks training program consisting of MP or MP with SS versus conventional rehabilitation techniques on cortical plasticity as assessed by TMS in individuals with incomplete cervical SCI.

Somatosensory stimulation consisted of trains of electrical stimulation delivered at 1 Hz, each train consisted of 5 single pulses at 1ms duration delivered at 10 Hz with stimulus intensity just below that which evoked an observable twitch in any of the muscles innervated by the median nerve.

These parameters were chosen because they preferentially activate large cutaneous and proprioceptive sensory fibers and because they were successfully used in prior studies modulating motor performance (**16,17,18).**

Also preliminary experiments found that a period of mixed nerve stimulation lasting at least 1.5 hours was necessary to produce reliable and significant increases in the size of MEP's evoked in small hand muscles **(16).**

Ridding and his colleagues **(16)** investigated the effect of prolonged peripheral nerve stimulation on 10 normal subjects. Two hours stimulation of the ulnar nerve induced a specific and significant increase in the size of MEP's evoked in hand muscles by TMS. There was no significant difference in the MT or the latencies.

In our study, comparison between pre and post-treatment TMS measures in group I, and II revealed, a significant decrease in the MT while there was no significant difference in group III.

On comparing the 3 groups together there was no significant difference between them regarding the MT, amplitude and latency. But it was evident that group I and II showed a greater decrease in the MT than group III but the difference was not of statistical significance.

Our results agreed with Beekhuizen and Field-Fote**(11)**who studied the effect of MP versus MP+SS on cortical plasticity in ten subjects who were assigned to either MP or MP+SS. Median nerve stimulation (500 ms train, 10 Hz, 1 ms pulse duration) was delivered. Training sessions were 5 d/week for 3 weeks at 2 h/session. Outcome measures included MT and MEP latency and amplitude. They found no significant between-groups differences regarding the MT but patients in MP+SS group demonstrated more decrease in MT than the MP group. Similarly, the statistical analysis identified no significant difference between pre and post-treatment MEP amplitude measures in the MP+SS group or in the MP group.

Beekhuizen and Field-Fote (2008)**(1)**identified a significant inter-groups difference for the MT, both in the MP+SS group and the MP group differed significantly from the control group.

Our failure to identify a significant difference between the groups regarding the changes in the TMS parameters (representing cortical excitability) might be due to the possibility that other aspects of cortical excitability not examined in this study may have changed due to the interventions.

We were not able to measure changes in the cortical maps in response to our treatment. If the cortical maps do change, then alterations in cortical excitability may be missed when the post-treatment measurement is taken in the same location as the pretesting measurement. In our study we used the same measurement site before and after training. Although the TMS coil used in this investigation would certainly evoke responses from a large area, it is likely that in the presence of a shift in the cortical map of the magnitude observed in the EEG studies by Green and his colleagues **(4)** the site of maximal excitability may well have been missed.

This was supported by the findings of Hoffman and Field-Fote study**(12)**, in which there was no change in the MT before and after the treatment, however the area of the cortical map increased by 8 additional sites.

Liepert and his colleagues **(19)** used TMS to map the cortical motor output area of a hand muscle on both sides in 13 stroke patients in the chronic stage of their illness before and after a 12-day-period of MP.

Before treatment, the cortical representation area of the affected hand muscle was significantly smaller than the contralateral side. After treatment, the muscle output area size in the affected hemisphere was significantly enlarged, corresponding to a greatly improved motor performance of the paretic limb. In follow-up examinations up to 6 months after treatment, motor performance remained at a high level, whereas the cortical area sizes in the 2 hemispheres became almost identical, representing a return of the balance of excitability between the 2 hemispheres toward a normal condition.

Studying 12 patients with chronic stroke before and after participation in 12 days of MP revealed that TMS showed significant increase in the amplitude of the MEP's and significant decrease in the MT (**20**).

Tarrka and his colleagues **(21)** studied the effect of MP in 13 patients with stroke on the cortical excitability. After 2 weeks of an intensive rehabilitation program, there was a significant increase in the amplitude of the MEP's produced by TMS after the intervention.

The study of Ragae and his colleagues **(22)** included 30 stroke patients. Patients were divided into 2 groups: group A received conventional rehabilitation program 3 times/week for 4 months and group B received CIMT 2 hr/day for 2 consecutive weeks. The results revealed a statistically highly significant difference in the mean of all scores in group B compared to group A. Also there was improvement in MT and the amplitude of the MEP's produced by TMS but not of statistical significance.

**5. Conclusion:**

The results of our study suggest that the combination of MP and SS results in changes in the cortical excitability in patients with SCI manifested in the MT needed to elicit the MEP's.

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