Altered Sensorimotor Integration With Cervical Spine Manipulation

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Abstract

Objective: This study investigates changes in the intrinsic inhibitory and facilitatory interactions within the sensorimotor cortex subsequent to a single session of cervical spine manipulation using single- and paired-pulse transcranial magnetic stimulation protocols.

Method: Twelve subjects with a history of reoccurring neck pain participated in this study. Short interval intracortical inhibition, short interval intracortical facilitation (SICF), motor evoked potentials, and cortical silent periods (CSPs) were recorded from the abductor pollicis brevis and the extensor indices proprios muscles of the dominant limb after single- and paired-pulse transcranial magnetic stimulation of the contralateral motor cortex. The experimental measures were recorded before and after spinal manipulation of dysfunctional cervical joints, and on a different day after passive head movement. To assess spinal excitability, F wave persistence and amplitudes were recorded after median nerve stimulation at the wrist.

Results: After cervical manipulations, there was an increase in SICF, a decrease in short interval intracortical inhibition, and a shortening of the CSP in abductor pollicis brevis. The opposite effect was observed in extensor indices proprios, with a decrease in SICF and a lengthening of the CSP. No motor evoked potentials or F wave response alterations were observed, and no changes were observed after the control condition.

Conclusion: Spinal manipulation of dysfunctional cervical joints may alter specific central corticomotor facilitatory and inhibitory neural processing and cortical motor control of 2 upper limb muscles in a muscle-specific manner. This suggests that spinal manipulation may alter sensorimotor integration. These findings may help elucidate mechanisms responsible for the effective relief of pain and restoration of functional ability documented after spinal manipulation. (J Manipulative Physiol Ther 2008;31:115-126)

Key Indexing Terms: *Manipulation; Spinal; Neuronal Plasticity; Transcranial Magnetic Stimulation; Neural Inhibition; Central Nervous System; Chiropractic*

The effectiveness of spinal manipulation in the treatment of acute and chronic low back pain has been well established in outcome-based research.[1,2] However, the mechanisms responsible for the effective relief of pain and restoration of functional ability after spinal manipulation are not well understood. Recent research suggests that joint dysfunction after injury may lead to maladaptive central changes that cause ongoing pain and loss of function, as alterations in somatosensory processing and sensorimotor integration have been demonstrated with cervical spine manipulation.[3]

It is well known that the adult human central nervous system (CNS) retains its ability to reorganize itself in response to altered afferent input.[4-9] Neural plastic changes take place after both increased[5,7] and decreased[4,6,8-10] afferent input. These plastic changes have been shown to alter CNS function that outlasts the period of the altered input.[11-13] It is also well known that pain can lead to central plastic changes throughout the entire core of the sensorimotor brain.[14]

Several studies have found evidences that suggest spinal dysfunction may lead to altered afferent input to the CNS.[15-19] This has led to the hypothesis that such altered afferent input may lead to central neural plastic changes.[20] Furthermore, it has been proposed that spinal manipulation, aimed at improving joint dysfunction, should be able to reverse this effect.[20] These authors have recently demonstrated altered

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cortical processing for 20 minutes after spinal manipulation of dysfunctional cervical joints in subjects with chronic neck complaints.[20]

The altered central processing observed in this subject group after spinal manipulation occurred only at the level of the cortex, with altered N20 and N30 somatosensory evoked potential (SEP) peak amplitude changes.[20] The N20 SEP peak is known to be generated in the primary somatosensory cortex (S1), whereas the N30 SEP peak is thought to reflect sensorimotor integration[21] in a more complex cortical and subcortical loop linking the basal ganglia, thalamus, premotor areas, and primary motor cortex.[22-26] Further support for cortical processing changes occurring after spinal manipulation has been obtained in a second study,[27] where the same authors have shown a shortening of the transcranial magnetic stimulation (TMS) induced cortical silent period (CSP) lasting on average 20 minutes postmanipulations.

The CSP is known to reflect both cortical and spinal inhibitory mechanisms.[28-33] Although spinal reflexive changes have been shown previously after spinal manipulation,[17,34,35] the CSP changes observed in this study lasted on average for 20 minutes. Furthermore, the authors found no changes in F responses, reflecting the antidromic excitability of a portion of the motoneuron pool.[36,37] They therefore concluded that although there may initially be some spinal reflexive changes, these lasting alterations observed with the CSP are most likely due to cortical inhibitory mechanisms. This current study sought to further investigate the acute neurophysiological effects of cervical spine manipulation using TMS by measuring several different types of inhibitory and facilitatory interactions within the sensorimotor cortex. Using various single- and paired-pulse TMS protocols, it is possible to measure alterations in processing within several different intracortical inhibitory and facilitatory pathways.[38-41] For this study, we measured CSPs, short interval intracortical inhibition (SICI), motor evoked potentials (MEPs), and short interval intracortical facilitation (SICF), also known as *I-wave facilitation* (IwF), in 2 different upper limb muscles.

Methods

Subjects

Twelve subjects participated in this study, including 5 women and 7 men aged 19 to 45 (mean age, 27.1 ± 7.7 years). All of the subjects were deemed to be right-handed (mean laterality quotient, 87.4%; range, 58.3%-100%) using the Edinburgh handedness questionnaire.[42] To be included, subjects could not have a history of neurologic disease, or any known contraindications to either spinal manipulation or magnetic stimulation (described in more detail below). The subjects were furthermore required to have a history of reoccurring neck pain or stiffness (eg, present during the performance of certain tasks such as work or study). However, at the time of the experiment, all subjects were required to be pain free. This was done to assess the potential effects of spinal manipulation delivered to dysfunctional joints alone without the presence of acute pain, as the presence of pain is known to alter corticomotor measures such as those used in this current study.[43-45] The University of Auckland Human Participants Ethical Committee approved the study in accordance with the Declaration of Helsinki.

Transcranial Magnetic Stimulation

Two MagStim 200 (MagStim, Dyfed, United Kingdom) magnetic stimulators and a 55-mm-diameter figure-of-8 coil were used to deliver single-pulse magnetic stimuli and double-pulse stimuli via a BiStim^2 unit (MagStim) over the cortical motor strip opposite to the dominant limb at the optimal position for eliciting MEPs from the abductor pollicis brevis (APB). A purpose-made tight-fitting cotton cap marked with a 1-cm grid over M1 was initially positioned with reference to the vertex and used to locate the optimal site. This optimal site was then marked on the scalp to ensure identical placement of the coil throughout the experiment. The coil was held approximately 45° to the midline with the handle pointing posteriorly. With this coil orientation, the induced current in the brain is directed approximately perpendicular to the line of the central sulcus, a condition optimal for activating the corticospinal system transsynaptically.[46] Resting and active motor thresholds were determined. *Rest motor threshold* (RTh) was defined as the minimal stimulus intensity at which 5 of 10 consecutive stimuli evoked an MEP with an amplitude of at least 50 μV in APB muscle at rest. The *active motor threshold* (ATh) was defined as the minimal stimulus intensity at which 5 of 10 consecutive stimuli evoked an MEP with an amplitude of at least 100 μV in APB muscle while holding a weak isotonic background contraction (5%-10% maximal voluntary contraction [MVC]).

Electromyographic Recording

Surface electromyographic (EMG) recordings were made from the APB and extensor indices proprios (EIP) muscles of the dominant limb. Electrodes for APB were placed with the active electrode over the motor point and the reference electrode over the metacarpophalangeal joint. For EIP, the active electrode was placed over the muscle belly, approximately 1 cm proximal and medial from the styloid process of the ulnar when the arm is in the pronated position; and the reference electrode was placed 2 cm proximal to the active electrode, in a direction approximately 45° outward from the midline of the forearm when in the pronated position. The ground electrode was placed on the lateral epicondyle of the distal end of the humerus. The EMG signals were collected from 7-mm–diameter Hydrospot Ag/AgCl electrodes (Physiometrix Inc, Billerica, MA) fixed with tape 1 cm apart after standard skin preparation to reduce electrode impedance to less than 5 kΩ. The EMG signals were amplified by a Grass Model 15 Neurodata acquisition system via an IMEB Model Bio-Potential Isolator Electrical Board

(Grass Technologies, West Warwick, RI), band-pass filtered at 30 Hz to 1 kHz (−6 dB cutoff points), sampled at a rate of 2 KHz by a LabView acquisition system and displayed using a custom-made LabView program (National Instruments, Austin, TX), and stored to disk for off-line analysis.

MEP and CSP Duration

The MEPs and CSPs were recorded with APB and EIP both holding a 5% to 10% background contraction. Stimulus intensity was set to 150% ATh for APB. The level of contraction was standardized across subjects for the APB and EIP muscles by determining the MVC for each subject. The root mean square (RMS) level of the EMG was obtained during a 3-second MVC obtained individually from both the target muscles (the best of 3). The limits for the EMG were then set at 5% and 10% of the maximum RMS level during the MVC. The RMS level of contraction was displayed in real time to provide feedback and assist the subject in maintaining the appropriate level of contraction in both muscles simultaneously. A stimulus was triggered by the computer only when the RMS level was maintained by both APB and EIP within their individual range for 1.5 seconds.

Short Interval Intracortical Inhibition

Short interval intracortical inhibition was studied by a paired TMS paradigm described by Kujirai et al[38] with a subthreshold conditioning stimulus (CS_{50}) followed by a suprathreshold test stimulus (TS). The TS intensity was adjusted to produce a peak-to-peak MEP amplitude of 1 mV (0.8-1.2 mV range accepted) from the relaxed APB. The CS_{50} was adjusted to provide 50% suppression of the TS MEP amplitude in the relaxed APB to avoid any "floor" or "ceiling" effects.[47,48] The interstimulus interval (ISI) was set at 2.5 milliseconds, as this has been shown to produce maximal SICI.[48,49] Sixteen trials of the TS alone, 16 trials of CS_{50} alone, and 16 trials of CS_{50} + TS were performed before and after the 2 interventions.

Short Interval Intracortical Facilitation

Short interval intracortical facilitation was studied with a paired-pulse paradigm similar to those previously described[39,50] with a suprathreshold TS (S1) followed by a subthreshold second stimulus (S2). The S1 was identical to the TS of SICI (to produce a peak-to-peak MEP amplitude of 0.8-1.2 mV in the relaxed APB). The intensity for S2 was set at 90% of RTh for APB. The ISI was set at 1.5 milliseconds. Sixteen trials of S1 alone, 16 trials of S2 alone, and 16 trials of S1 + S2 were performed before and after the 2 interventions.

F Waves

To assess spinal motor excitability, F waves were recorded from the subjects' relaxed APB. The median nerve was stimulated at the wrist with a supramaximal (1.25 Mmax, i.e. 25% above the lowest intensity that elicited a maximal M wave) electrical stimulation consisting of square-wave constant current pulses with pulse width duration of 0.2 milliseconds, as recommended in the literature.[36,37] Twenty trials were recorded for each subject before and after each intervention. The F wave amplitudes were expressed as a percentage of the M wave amplitude. The F wave persistence was expressed as a percentage of F waves present in the 20 trials recorded.

Spinal Manipulation Intervention

This intervention consisted of spinal manipulation of the subjects' dysfunctional cervical joints, which were determined by a registered chiropractor. The clinical evidence of joint dysfunction includes tenderness to palpation of the relevant joints, restricted intersegmental range of motion, palpable asymmetric intervertebral muscle tension, abnormal or blocked joint play and end-feel of a joint, and sensorimotor changes in the upper extremity.[51,52] The most reliable spinal dysfunction indicator is tenderness with palpation of the dysfunctional joint.[53,54] Cervical range of motion[55,56] has also been shown to have good inter- and intraexaminer reliability. For the purpose of this study, *spinal dysfunction* was therefore defined as the presence of both restricted intersegmental range of motion and tenderness to palpation of the joint of at least one cervical spine segment. This was detected in the following manner. The examiner, a registered chiropractor with at least 7 years of clinical experience, would passively move the subject's head, while palpating and stabilizing over the zygapophyseal joints. For each spinal segment, the head would be gently and passively moved from the neutral position to the maximal range of lateral flexion in the coronal plane, to both the left and the right. If this movement appeared restricted, the examiner would apply gentle pressure to the joint, while watching for signs of discomfort from the subject. The examiner would also ask the subject if the pressure to the joint elicited pain. Spinal segments that were deemed both to be restricted in lateral flexion range of motion and to elicit pain on palpation were defined for the purpose of this study to be *dysfunctional*.

The spinal manipulations carried out in this study were high-velocity, low-amplitude thrusts to the spine held in lateral flexion, with slight rotation and slight extension. This is a standard manipulative technique used by manipulative physicians, physiotherapists, and chiropractors. The mechanical properties of this type of CNS perturbation have been investigated; and although the actual force applied to the subject's spine depends on the therapist, the patient, and the spinal location of treatment, the general shape of the force-time history of spinal manipulation is very consistent[57] and the duration of the thrust is always less than 200 milliseconds.[58] The high-velocity type of manipulation was chosen specifically because previous research[59] has shown that reflex EMG

activation observed after manipulation only occurred after high-velocity, low-amplitude manipulations (as compared with lower-velocity mobilizations) and would therefore be more likely to alter afferent input to the CNS and lead to measurable TMS evoked potential changes.

Control Intervention

The control intervention consisted of a passive movement of the subject's head that was carried out by the same chiropractor who had prechecked the subjects for spinal dysfunction and who performed the spinal manipulations for the spinal manipulation experiment. The passive head movement control intervention involved the subject's head being passively laterally flexed, and slightly extended and rotated to a position that the chiropractor would normally manipulate that person's cervical spine and then returning the subject's head back to neutral position. This was repeated to both the left and the right. However, the experimenter was particularly careful not to put pressure on any individual cervical segment. Loading a joint, as is done before spinal manipulation, has been shown to alter paraspinal proprioceptive firing in anesthetized cats[60] and was therefore carefully avoided by ending the movement before end range of motion when passively moving the subjects' heads. No spinal manipulation was performed during any passive head movement experiment. The passive head movement experiment was not intended to act as a sham manipulation but as a physiological control for possible changes occurring because of the cutaneous, muscular, or vestibular input that would occur with the type of passive head movement involved in preparing a subject/patient for a cervical manipulation. It also acted as a control for the effects of the magnetic stimulation necessary to collect the dependent measures of the study.

Experimental Protocol

Subjects were first given written and verbal information, and informed consent was obtained. All the subjects' cervical spines were first checked by a registered chiropractor to determine if and where their spines would be manipulated. If the subjects were judged to have cervical spine dysfunction, the relevant information (including detailed medical history) was then obtained. All subjects were also screened for evidence of vertebral artery ischemia, with their head in a position of extension, lateral flexion, and rotation, which are neck positions shown to have the greatest mechanical stress to the contralateral vertebral artery.[61] Subjects were also screened for other contraindications for cervical manipulation, such as recent history of trauma, known conditions such as inflammatory or infectious arthropathies, or bone malignancies. Finally, subjects were screened for contraindications for magnetic stimulation, such as a history of epilepsy, pregnancy, or metal implants in the brain.

Baseline experimental measures (ATh, RTh, MEPs, CSPs, SICI, SICF, and F and M waves, all described in detail above) were then recorded before and after either the passive head movement control intervention or the spinal manipulation intervention. The various measures were recorded in a randomized order. The order that the 2 interventions were carried out was also randomized. If the subject was to receive the spinal manipulation intervention before the control, the 2 recording sessions were carried out on different days with at least 4 weeks in between.

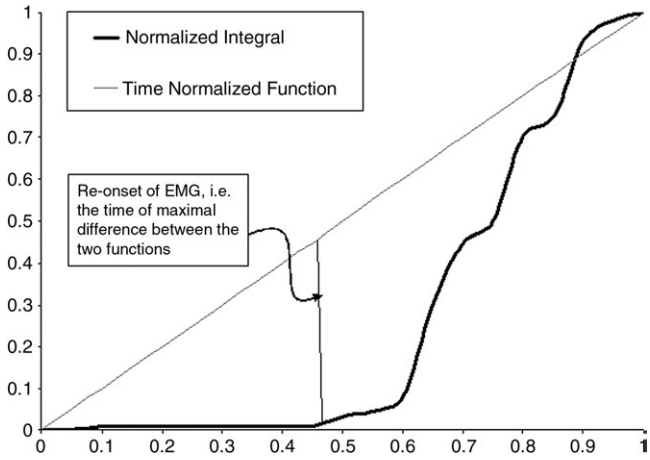

Fig 1. *Graph of normalized integral and time normalized function demonstrating the time of maximal difference between the two, which will be the time chosen to represent reonset of EMG for CSP duration calculations.*

Data Analysis

The peak-to-peak amplitudes of the 16 MEPs per trial were averaged for statistical analysis. For increased objectivity in the data analysis process, the CSP duration was also determined using a LabView computer program written to measure the time from TMS stimulation to reonset of EMG. Reonset of EMG was determined using the integrated profile method[62] implemented in LabView. The integrated profile method first integrates the EMG data over time. A function was created representing the integral of the signal from the start of the data to each time point. This function was amplitude normalized using the total integral value. A second function was created representing a signal with an integral equally distributed over time. The *reonset of EMG* was defined as the time at which there was maximal difference between these 2 functions (Fig 1). To avoid the effect of the MEP peaks on the reonset determination, the user visually places a cursor after the MEP peaks; and the signal from the cursor onward is used in the integrated profile method. As long as the cursor was placed anywhere in the first half of the silent period, the CSP calculations were consistent. The 16 CSPs were averaged for each trial for statistical analysis.

The median nerve stimulation EMG traces were inspected visually for the presence of F waves. If present,

Table 1. *Average RTh (percentage of maximum stimulator output (%MSO) ± SD) and ATh (percentage MSO ± SD) data for the pre- and postcontrol as well as the pre- and postmanipulation for both the APB and EIP muscles*

	Precontrol	Postcontrol	Premanipulation	Postmanipulation
APB				
RTh (%MSO) ± SD	45.9 ± 6.6	46.0 ± 6.9	45.4 ± 6.9	46.1 ± 7.0
ATh (%MSO) ± SD	37.8 ± 6.7	37.8 ± 6.7	37.5 ± 6.8	37.9 ± 6.8
EIP				
RTh (%MSO) ± SD	44.6 ± 7.9	45.1 ± 7.6	44.8 ± 7.6	45.3 ± 7.6
ATh (%MSO) ± SD	37.6 ± 7.3	37.5 ± 7.0	36.8 ± 6.9	37.0 ± 7.0

Table 2. *The average median nerve F wave amplitude (expressed as F wave to M response ratio ± SD), the average M wave amplitude (millivolts ± SD), and the average F wave persistence (percentage of 20 ± SD) data for the pre- and postcontrol as well as the pre- and postmanipulation for both the APB and EIP muscles*

	Precontrol	Postcontrol	Premanipulation	Postmanipulation
F wave amplitude to M response ratio	0.031	0.029	0.026	0.036
F wave persistence (%) ± SD	50 ± 16	53 ± 20	50 ± 18	46 ± 34
M response (mV) ± SD	17.7 ± 6.5	17.6 ± 6.5	18.03 ± 5.0	17.7 ± 4.7

their peak-to-peak amplitudes (in millivolts) were determined and averaged per subject both before and after both interventions. The peak-to-peak amplitudes (in millivolts) of the M waves were also determined, and the mean F wave amplitude was expressed as a percentage of the M wave for statistical comparisons.

The SICI was expressed as the percentage decrease in the mean MEP amplitude after paired-pulse TMS compared with the mean MEP amplitude after single magnetic pulses (the TS) ($100 - [(CS_{50} + TS/TS) * 100]$). The SICF was expressed as the percentage increase in the mean MEP amplitude after paired-pulse TMS compared with the mean MEP amplitude after single magnetic pulses (S1 alone = the TS) ($[S1S2/S1 * 100] - 100$).

For statistical analysis, repeated-measures analysis of variance (ANOVA) was applied separately for each of the measured parameters as follows. Initially, for the RTh, ATh, MEP, CSP, SICF, and SICI data, 2-way ANOVAs for repeated measures with the factors "muscle" and "intervention" were applied to compare the effects of spinal manipulation on the 2 different upper limb muscles. Where significant, 1-way repeated-measures ANOVAs were applied separately for each muscle with "intervention" as the factor. One-way repeated-measures ANOVAs were also applied separately for the M wave amplitude and each of the F wave parameters with "intervention" as factor. Two-tailed paired *t* tests were applied where applicable. The significance level was set to $P < .05$.

Results

Control Intervention

There were no statistically significant changes observed in any of the experimental variables after the passive head movement control intervention (Tables 1, 2, 3, and 4).

Spinal Manipulation Intervention

Rest and active motor threshold showed no statistically significant changes after this intervention (Table 1). Neither were there any significant changes to the F wave parameters measured (F wave amplitude and persistence) (Table 2) or M wave amplitudes (Table 2).

For the SICI data, a significant effect of the factor "muscle" was observed ($F [1, 44] = 4.46$, $P = .04$). There was also a significant interaction effect for the factors "muscle" and "intervention" ($F [1, 44] = 5.10$, $P = .03$). The 1-way repeated-measures ANOVA revealed a significant effect for the factor "intervention" only for the APB ($F [1, 22] = 6.59$, $P = .02$). The 2-tailed paired *t* tests revealed a significant decrease of SICI in the APB muscle ($P = .02$) (Fig 2 and Table 3). There were no significant alterations of SICI after the control intervention.

For the SICF data, a significant effect of the factor "muscle" was observed ($F [1, 44] = 4.35$, $P = .04$). There was also a significant interaction effect for the factors "muscle" and "intervention" ($F (1, 44) = 9.18$, $P = .004$). The 1-way repeated-measures ANOVA revealed a significant effect for the factor "intervention" for both the APB ($F [1, 22] = 4.70$, $P = .04$) and EIP data ($F [1, 22] = 5.96$, $P = .02$). The 2-tailed paired *t* tests revealed a significant increase of SICF in the APB muscle ($P = .003$) and a significant decrease of SICF in the EIP muscle after spinal manipulation ($P = .001$) (Fig 3 and Tables 3 and 4). There were no significant alterations of SICF after the control intervention.

For the CSP data, a significant effect of the factor "muscle" was observed ($F [1, 42] = 4.27$, $P = .05$). There was also a significant interaction effect for the factors "muscle" and "intervention" ($F [1, 42] = 4.32$, $P = .040$). The 1-way repeated-measures ANOVA revealed a significant effect of the factor "intervention" for the APB ($F [1, 2] = 4.74$, $P = .04$). For the EIP data, there was only

Table 3. *Average pre- and postcontrol as well as pre- and postmanipulation MEP (millivolts ± SD), CSP (milliseconds ± SD), S1 (millivolts ± SD), S1 + S2 (millivolts ± SD), S2 (millivolts ± SD), percentage IwF ([S1S2/S1 *100] − 100), TS (millivolts ± SD), CS_{50} + TS (millivolts ± SD), CS_{50} (millivolts ± SD), and percentage SICI (100 − [(CS_{50} + TS/TS) *100]) data for the APB muscle*

	Precontrol	Postcontrol	Premanipulation	Postmanipulation
MEP amplitude (mV) ± SD	5.2 ± 1.9	5.1 ± 1.6	4.5 ± 2.7	4.3 ± 2.5
CSP duration (ms) ± SD	185.3 ± 25.7	189.0 ± 23.5	188.4 ± 34.7	178.2 ± 36.9 *
S1 (mV) ± SD	0.99 ± 0.2	0.86 ± 0.3	1.02 ± 0.2	1.07 ± 0.4
S1 + S2 (mV) ± SD	1.6 ± 0.5	1.4 ± 0.5	1.7 ± 0.6	2.1 ± 1.1
S2 (mV) ± SD	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01
IwF (% increase above S1 alone)	65.9 ± 29.3	63.9 ± 23.2	66.6 ± 51.2	92.5 ± 58.9 *
TS (mV) ± S	1.04 ± 0.2	0.91 ± 0.2	1.02 ± 0.2	1.05 ± 0.5
CS_{50} + TS (mV) ± SD	0.53 ± 0.1	0.44 ± 0.1	0.52 ± 0.1	0.72 ± 0.3
CS_{50} (mV) ± SD	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01
SICI (% less than TS alone)	48.0 ± 11.1	50.0 ± 13.1	47.9 ± 11.0	29.24 ± 22.0 *

* $P < .05$.

Table 4. *Average pre- and postcontrol as well as pre- and postmanipulation MEP (millivolts ± SD), CSP (milliseconds ± SD), S1 (millivolts± SD), S1 + S2 (millivolts ± SD), S2 (millivolts ± SD), percentage IwF ([S1S2/S1 *100] − 100), TS (millivolts± SD), CS_{50} + TS (millivolts ± SD), CS_{50} (mV ± SD), and percentage SICI (100 − [(CS_{50} + TS/TS) *100]) data for the EIP muscle*

	Precontrol	Postcontrol	Premanipulation	Postmanipulation
MEP amplitude (mV) ± SD	2.0 ± 1.1	1.9 ± 1.2	1.9 ± 1.2	1.7 ± 1.1
CSP duration (ms) ± SD	172.6 ± 27.5	176.2 ± 24.4	183.4 ± 27.6	195.4 ± 24.5 *
S1 (mV) ± SD	0.45 ± 0.3	0.53 ± 0.4	0.48 ± 0.3	0.40 ± 0.2
S1 + S2 (mV) ± SD	0.72 ± 0.5	0.58 ± 0.4	0.64 ± 0.3	0.50 ± 0.2
S2 (mV) ± SD	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01
IwF (% increase above S1 alone)	43.3 ± 51.6	48.1 ± 52.0	46.1 ± 29.6	35.2 ± 26.8 *
TS (mV) ± S	0.44 ± 0.3	0.42 ± 0.3	0.45 ± 0.3	0.38 ± 1.1
CS_{50} + TS (mV) ± SD	0.26 ± 0.3	0.23 ± 0.2	0.26 ± 0.3	0.20 ± 0.2
CS_{50} (mV) ± SD	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01
SICI (% less than TS alone)	45.0 ± 21.8	46.24 ± 20.7	45.3 ± 22.5	50.3 ± 17.6

* $P < .05$.

a significant effect for the overall repeated measures (ie, overall pre- vs postintervention data) ($F [1, 21] = 4.80$, $P = .04$). The 2-tailed paired t tests revealed a significant shortening of the CSP in the APB muscle ($P = .01$) (Fig 4) and a significant lengthening of the CSP in the EIP muscle after spinal manipulation ($P = .01$) (Fig 5). There were no significant changes in CSP for either muscle after the control condition. The group average CSP data are shown in Tables 3 and 4.

Discussion

In the present study, we explored the possibility that specific intracortical inhibitory and facilitatory pathways are altered in a muscle-specific manner after spinal manipulation of dysfunctional spinal joints. The results of this study support this theory. The major finding in this study was that manipulation of dysfunctional cervical segments leads to a significant increase in SICF, a significant decrease in SICI, and a significant shortening of the CSP in the APB muscle. Furthermore, cervical manipulations lead to the opposite effects in the EIP muscle, with a significant decrease in SICF and a lengthening of the CSP. To our knowledge, no prior study has shown selective changes in SICF, SICI, and CSP after spinal manipulation.

The CSP

The reduced CSP in APB after cervical spine manipulation is consistent with our previous study.[27] This may reflect altered intracortical inhibition. The CSP is known to reflect both spinal and cortical inhibitory components.[28-33] Studies have shown that the first part of the CSP (about 50 milliseconds) after transcortical stimulation is produced mainly by spinal mechanisms such as after-hyperpolarization and Renshaw recurrent inhibition of the spinal motoneurons.[28,29] Reciprocal inhibitory effects on the target muscle may also contribute because the magnetic stimulation often causes simultaneous activation of antagonists. However, the rest of the CSP (after about 50 milliseconds) is produced mainly by cortical inhibition.[28-33]

The exact mechanisms of the cortical inhibition responsible for producing the CSP are however more difficult to establish. Most evidence suggests that this inhibition is presynaptic to the corticospinal neurons, rather than due to a

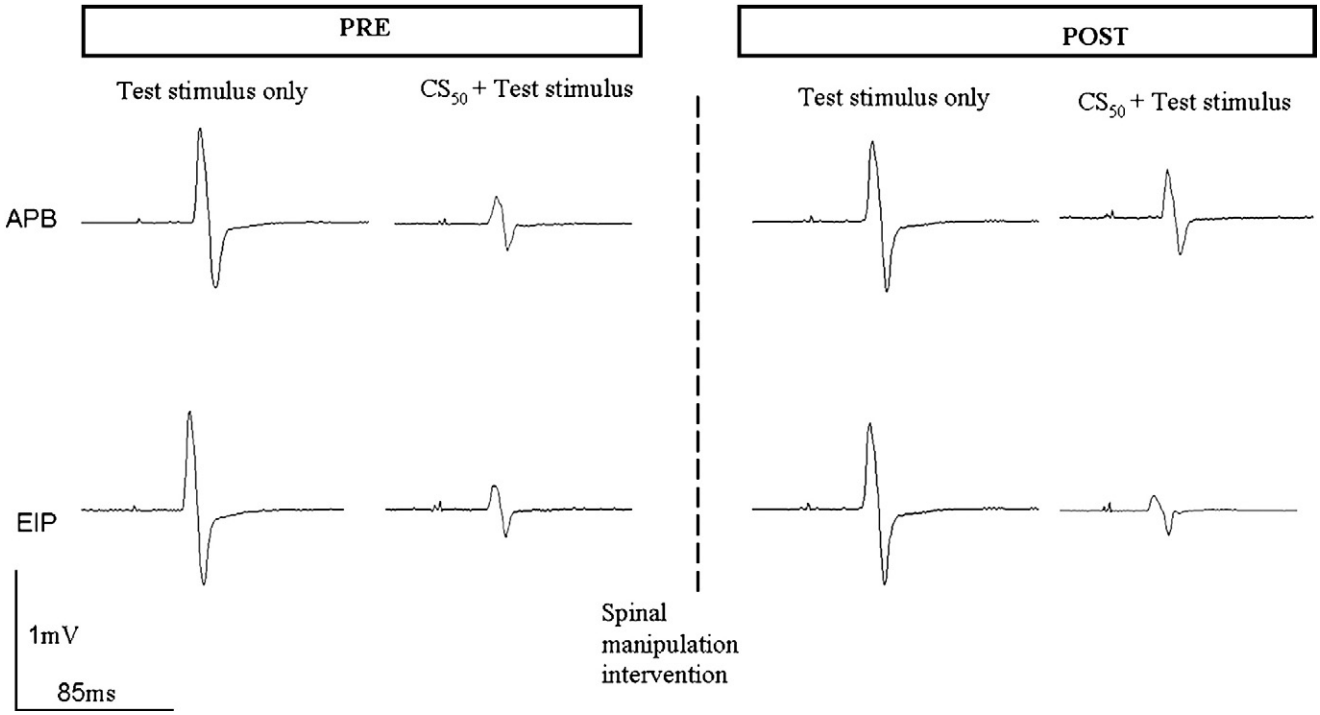

Fig 2. *Raw nonrectified EMG traces from one representative subject showing the pre- and postmanipulation TS and CS_{50} + TS MEPs for both the APB and EIP muscles. Note the decrease in SICI (ie, less inhibition of MEP in the CS_{50} + TS compared with premanipulation MEP) for the APB muscle.*

decreased excitability of these corticospinal neurons (which would be reflected by a decreased MEP).[29,30,63] Neuropharmacological modulation in healthy subjects suggest that the CSP reflects gamma-aminobutyric acid $(GABA)_B$-mediated intracortical inhibition.[64,65] Some have argued that it results from activation of inhibitory neurons projecting onto the pyramidal cells of the motor cortex.[29] However, it may also reflect a withdrawal of excitatory input to pyramidal cells by increased inhibition of such excitatory pathways.

Spinal reflexive changes have been previously demonstrated after spinal manipulation.[17,34,35] These spinal reflexive changes are short-lived, but can be measured in distant muscles.[34] The CSP changes observed in the current study, as well as our previous study,[27] have demonstrated that the alterations in intracortical inhibition after spinal manipulation lasted for at least 10 to 20 minutes after the manipulations. No long-lasting changes in the median nerve F responses were observed. The F wave properties reflect the antidromic excitability of a portion of the motoneuron pool,[36,37] suggesting that no lasting changes in spinal excitability occur after spinal manipulation. This is also in agreement with previous research.[17,34,35] The CSP changes observed in this study are therefore thought to reflect a reduction of intracortical inhibition of the APB and an increase in intracortical inhibition of the EIP, although initial short-lived spinal reflexive changes cannot be ruled out. Such potential short-lived spinal reflexive changes may even play a role in initiating the alterations in cortical excitability observed in this study.

Intracortical Facilitation

The protocol used in the current study to measure SICF (also known as *IwF*) with a suprathreshold first stimulus (S1), a subthreshold second stimulus (S2), and an ISI of 1.5 milliseconds is known to reflect the function of intracortical facilitatory circuits[39-41] and is reduced by drugs that enhance GABAergic function.[66,67]

The current study results suggest that cervical manipulation of patients with chronic neck complaints may lead to subtle alteration in motor control of upper limb muscles in a muscle-specific manner. The participants of this study had ongoing neck problems, although they were not in acute pain at the time of the study. It may be that an initial injury, and the presence of pain, has led to subtle motor control changes that in turn may have perpetuated their problem and led to either chronic neck pain or reoccurring neck pain superimposed on a background of neck stiffness. Episodes of acute pain, such as after an injury, are well known to induce plastic changes that can progressively lead to functional, structural, neurochemical, and molecular changes throughout the entire core of the sensorimotor brain.[14] It is already known that, with both insidious-onset and trauma-induced chronic neck pain conditions, there is impairment of deep cervical neck flexors and significant postural disturbances

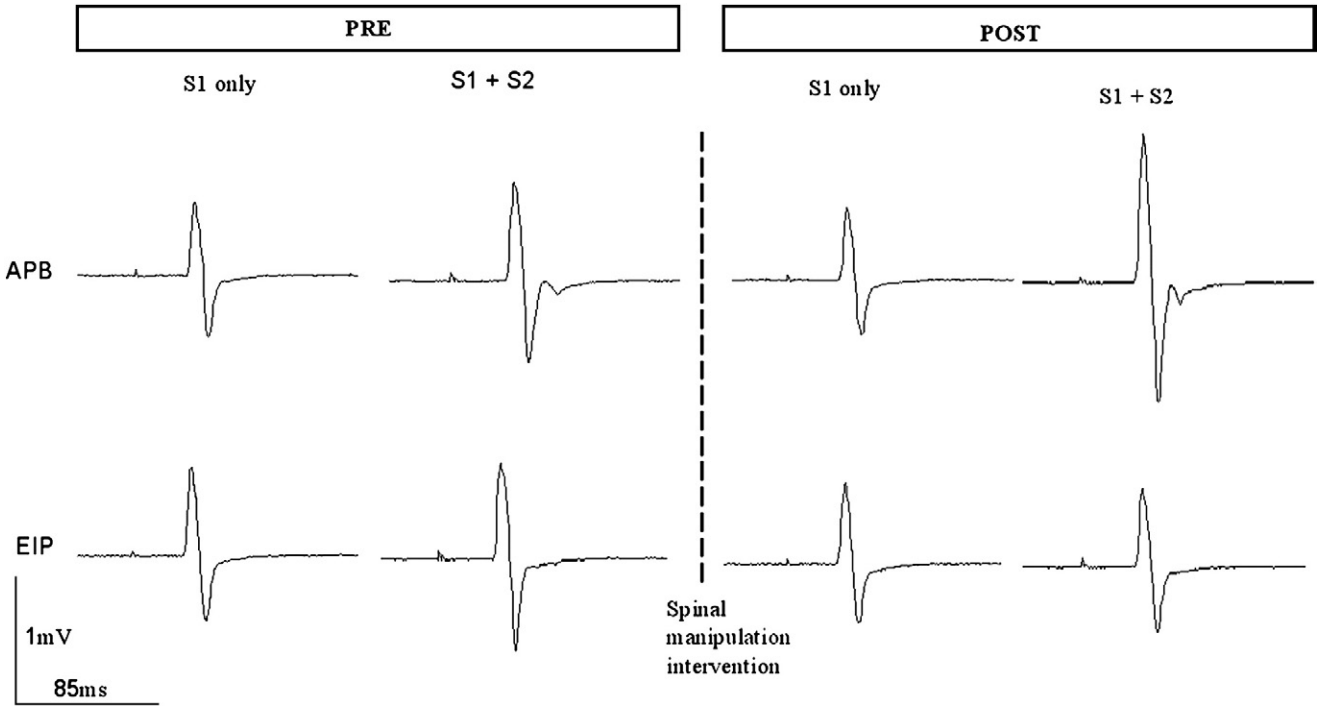

Fig 3. *Raw nonrectified EMG traces from one representative subject showing the pre- and postmanipulation S1 and S1 + S2 MEPs for both the APB and EIP muscles. Note the increase in SICF for the APB muscle and the decrease in SICF for the EIP muscle after the motor training session.*

during walking and standing.[68-74] Altered sensitivity of proprioceptors within the neck muscles has been suggested to be related to the postural disturbances seen in these patients.[70,74] There is also evidence to suggest that muscle impairment occurs early in the history of onset of neck pain[75] and that this muscle impairment does not automatically resolve even when neck pain symptoms improve.[75,76] Some authors have therefore suggested that the deficits in proprioception and motor control, rather than neck pain itself, may be the main factors defining the clinical picture and chronicity of different chronic neck pain conditions.[74]

It is possible that these deficits in proprioception and motor control may be partly due to spinal dysfunction, causing either inhibition or facilitation of neural input to the related muscles. Furthermore, in addition to the known changes that occur in deep cervical flexors and postural muscles, it is possible that subtle motor control changes may also develop in forearm and hand muscles. There is some evidence in the literature that upper limb extensor muscles are controlled in a different manner compared with flexors.[77,78] While recording EMG from the wrist and finger muscles in macaque monkeys, intracortical microstimulation of their motor cortex has demonstrated that inhibition appears most commonly in their flexor muscles, whereas facilitation was generally stronger in extensors.[78] Furthermore, a more recent functional magnetic resonance imaging study has also suggested that there are differences in the cortical control of flexors and extensors of the upper extremity of humans.[77] It has also been demonstrated that activation of upper limb pain fibers gives rise to complex modulatory effects on upper limb motoneuron pools.[45] Aδ fibers initiate a spinal reflex resulting in MEP amplitude reduction in muscles involved in reaching and grasping and in MEP amplitude facilitation in muscles involved in withdrawal.[45] The authors of this study concluded that their findings suggest a protective reflex mediated by Aδ fibers that protects the hand from harm.[45] It is therefore possible that an original neck and/or upper limb injury could lead to an overactive facilitation and/or underactive inhibition of forearm extensors, and an underactive facilitation and/or overactive inhibition of forearm flexors and intrinsic hand muscles such as APB. This would explain the findings in our participants.

A recent study has demonstrated a pathophysiological link between neck muscle fatigue and impaired postural control and demonstrated that physiotherapy treatment, including passive and active mobilization, could relieve the symptoms of impaired neck muscle function by reducing fatigability.[79] Furthermore, as mentioned earlier, it has recently been demonstrated using SEPs that cortical processing of upper limb information (median nerve transcutaneous stimulation) changes for at least 20 minutes after spinal manipulation of dysfunctional cervical vertebrae in patients with chronic neck complaints.[20] The muscle-

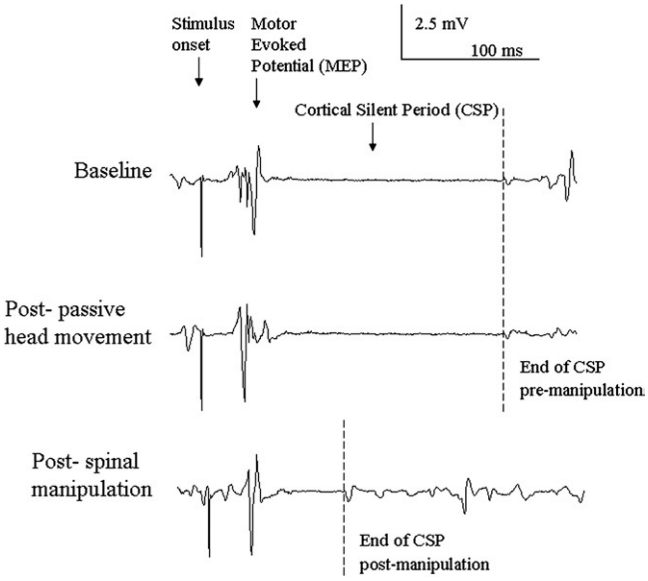

Fig 4. *Raw nonrectified EMG traces from one representative subject showing baseline, postcontrol, and postmanipulation MEP and CSP for the APB muscle. Note the shortening of the CSP after manipulation.*

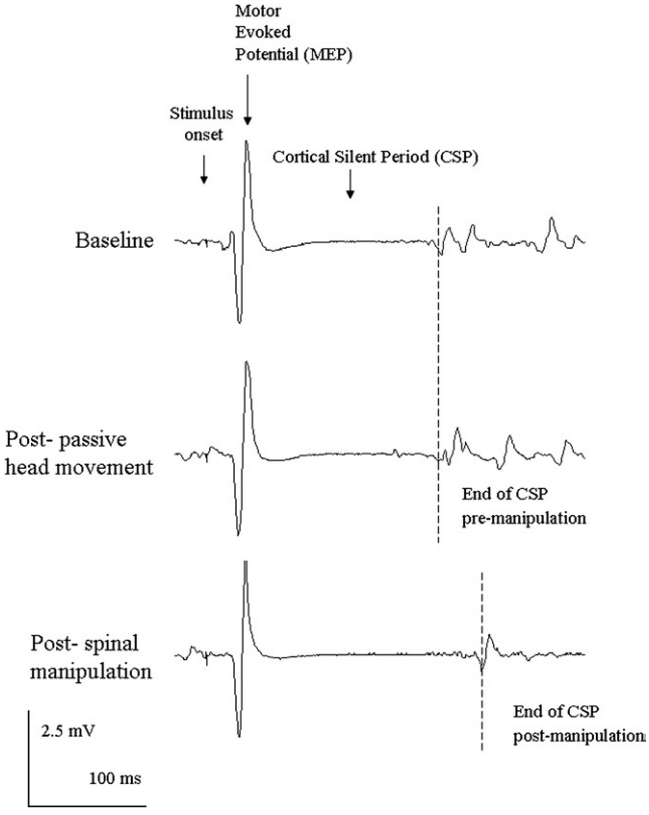

Fig 5. *Raw nonrectified EMG traces from one representative subject showing baseline, postcontrol, and postmanipulation MEP and CSP for the EIP muscle. Note the lengthening of the CSP after manipulation.*

specific alterations in SICF, SICI, and CSP duration observed after spinal manipulation of dysfunctional cervical vertebrae in the current study may reflect these same cortical changes.

Short Interval Intracortical Inhibition

Both SICF and SICI are predominantly affected by agents with effects at the $GABA_A$ receptor.[66,80,81] Short interval intracortical inhibition has been shown to be mediated through a low-threshold $GABA_A$ receptor–dependent inhibitory pathway,[81] and SICF has been shown to reflect a facilitatory I-wave interaction at the level of the motor cortex that is controlled by $GABA_A$ receptor–dependent inhibition.[66] $GABA_A$ receptor–mediated inhibition has been shown to be important in use-dependent plasticity.[82] Although SICF appears to operate by different mechanisms from SICI,[81] it is thought that a reduction of SICI could serve to "release" cortical representations from inhibition and focus subsequent excitatory drive to produce the intended movement.[83] The reduced SICI and increased SICF in APB observed in the current study therefore suggest that there is a down-regulation of $GABA_A$ receptor–mediated inhibition, with an accompanying release of intracortical I-wave facilitation to the APB muscle after spinal manipulation. The opposite effect may be present in the EIP muscle. However, although there was a trend toward an increased SICI in EIP and the group average increased postmanipulations, these did not reach statistical significance. There was however, as discussed above, a significant decrease in SICF in EIP postmanipulation, suggesting there is an up-regulation of $GABA_A$ receptor–mediated inhibition and resulting in the reduction of intracortical I-wave facilitation of EIP postmanipulations.

Potential Benefits of Spinal Manipulation in Chronic Neck Pain

Chronic neck pain is becoming increasingly prevalent in society. As many as 67% of individuals will have some form of neck pain at some stage in their life.[84] In the future, if spinal manipulation can be shown to systematically and reliably alter neural processing and abnormal motor control, it could play an important role in the rehabilitation of these chronic neck pain patients.

Episodes of acute pain, such as after an injury, may initially induce plastic changes in the sensorimotor system.[14] Pain alone, without deafferentation, has been shown to induce increased SEP peak amplitudes[85,86] and increased somatosensory evoked magnetic fields.[87] Research has also shown that the CSP is prolonged with experimentally induced tonic cutaneous pain.[44] Noxious stimuli applied to the digits have also been shown to result

in MEP amplitude reduction in muscles involved in reaching and grasping and in MEP amplitude facilitation in muscles involved in withdrawal, suggesting a pain-induced reflexive effect that protects the hand from harm.[45] Such plastic changes can become a "chronically progressive, functional, structural, and neurochemical/molecular make-over of the entire core of the somatosensory (and motor) brain" (Wall et al,[14] p 206). Phantom limb pain is an obvious example of a maladaptive chronic pain condition.[88] As sensorimotor disturbances are known to persist beyond the acute episode of pain[75,76] and are thought to play a defining role in the clinical picture and chronicity of different chronic neck pain conditions,[74] then the selective changes in SICI, SICF, and CSP observed in the current study after spinal manipulation may reflect a normalization of such injury-/pain-induced central plastic changes, which may reflect one mechanism for the improvement of functional ability reported after spinal manipulation.

Conclusions

The observations in the present study suggest that spinal manipulation of dysfunctional joints may modify transmission in neuronal circuitries not only at a spinal level as indicated by previous research,[17,34,35] but also at a cortical level as recently also demonstrated with SEPs.[20] The current study found selective muscle-specific changes in SICF, SICI, and CSP after spinal manipulation of dysfunctional cervical segments. These changes suggest that spinal dysfunction may lead to muscle-specific alterations in intracortical inhibitory and facilitatory processing and motor control. Furthermore, it suggests that one mode of action of spinal manipulation is to reverse such maladaptations in sensorimotor integration, thus impacting and improving motor control. Further studies are needed to elucidate the role and mechanisms of these cortical changes and their relationship to a patient's clinical presentation.

Practical Applications

- Spinal manipulation of dysfunctional cervical joints may alter specific central corticomotor facilitatory and inhibitory neural processing and cortical motor control of 2 upper limb muscles in a muscle-specific manner.
- This suggests that spinal manipulation may alter sensorimotor integration.
- These findings may help elucidate the mechanisms responsible for the effective relief of pain and restoration of functional ability documented after spinal manipulation.

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