Effects of 12 Weeks of Chiropractic Care on Central Integration of Dual Somatosensory Input in Chronic Pain Patients: A Preliminary Study

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Abstract

Objective: The purpose of this preliminary study was to assess whether the dual somatosensory evoked potential (SEP) technique is sensitive enough to measure changes in cortical intrinsic inhibitory interactions in patients with chronic neck or upper extremity pain and, if so, whether changes are associated with changes in pain scores.

Methods: The dual peripheral nerve stimulation SEP ratio technique was used for 6 subjects with a history of chronic neck or upper limb pain. SEPs were recorded after left or right median and ulnar nerve stimulation at the wrist. SEP ratios were calculated for the N9, N13, P14-18, N20-P25, and P22-N30 peak complexes from SEP amplitudes obtained from simultaneous median and ulnar stimulation divided by the arithmetic sum of SEPs obtained from individual stimulation of the median and ulnar nerves. Outcome measures of SEP ratios and subjects' visual analog scale rating of pains were recorded at baseline, after a 2-week usual care control period, and after 12 weeks of multimodal chiropractic care (chiropractic spinal manipulation and 1 or more of the following: exercises, peripheral joint adjustments/manipulation, soft tissue therapy, and pain education).

Results: A significant decrease in the median and ulnar to median plus ulnar ratio and the median and ulnar amplitude for the cortical P22-N30 SEP component was observed after 12 weeks of chiropractic care, with no changes after the control period. There was a significant decrease in visual analog scale scores (both for current pain and for pain last week).

Conclusion: The dual SEP ratio technique appears to be sensitive enough to measure changes in cortical intrinsic inhibitory interactions in patients with chronic neck pain. The observations in 6 subjects revealed that 12 weeks of chiropractic care improved suppression of SEPs evoked by dual upper limb nerve stimulation at the level of the motor cortex, premotor areas, and/or subcortical areas such as basal ganglia and/or thalamus. It is possible that these findings explain one of the mechanisms by which chiropractic care improves function and reduces pain for chronic pain patients. (J Manipulative Physiol Ther 2017;40:127-138)

Key Indexing Terms: *Somatosensory Evoked Potentials; Spinal Manipulation; Sensory Gating; Neuroplasticity; Transcutaneous Nerve Stimulation*

Introduction

Spinal manipulation is known to result in clinical improvements in spinal function and reduction of both acute and chronic low back and neck pain.[1-7] However, the mechanism(s) responsible for the restoration of function and relief of pain after manipulative care are not well understood. We have yet to fully understand the neurophysiological mechanisms responsible for such clinical improvements after spinal manipulation of any kind. It is of interest to us whether chiropractic care can induce changes in various aspects of central nervous system (CNS) functioning, including alterations in reflex excitability,[8-12] sensory processing,[13] and motor control.[12]

A recent study used the dual somatosensory evoked potential (SEP) ratio technique to further explore these CNS alterations following chiropractic adjustment/manipulation.[14,15] This experimental technique has previously been used by Tinazzi et al.,[16] who found that dystonic subjects exhibited an abnormality in the intrinsic inhibitory interactions within the somatosensory system. The technique can be used to measure central integration of dual somatosensory input.[16] This can be achieved by comparing the amplitudes of SEP peaks obtained

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by stimulating the median and ulnar nerves simultaneously (MU) with the amplitude obtained from the arithmetic sum of the SEPs elicited by stimulating the same nerves separately (M + U). The ratio of MU to M + U indicates the central interaction between afferent inputs from these 2 peripheral nerves and, thus, reflects the degree to which the CNS filters or gates excessive somatosensory afferent information.[17-21]

Previous research has indicated that healthy individuals have smaller central MU SEP amplitudes (ie, SEP amplitudes following MU) compared with the M + U amplitudes (ie, SEP amplitude calculated as the arithmetic sum of the individual median and ulnar SEPs).[16,22] However, in conditions such as dystonia[16] and Huntington's disease,[23] increased central SEP ratios have been observed. The increased SEP ratios suggest that these individuals receive distorted and excessive (ie, not spatially filtered) afferent input from their affected limb or limbs, which may potentially cause their motor system to transform these afferent inputs into abnormal "unhealthy" motor outputs. Sensorimotor disturbances are also known to persist beyond acute episodes of pain,[24,25] and such sensorimotor disturbances are thought to play a defining role in the clinical picture and chronicity of different chronic pain conditions.[26] We therefore hypothesized that patients with chronic pain may also have increased central dual SEP ratios.

Our previous studies using the SEP ratio technique examined the effects of cervical spine chiropractic manipulation (also known as chiropractic adjustments) and a period of repetitive muscular contractions.[14,22] This work demonstrated that the dual-peripheral-nerve-stimulation SEP technique may be used as a sensitive measure of sensorimotor integration (SMI). The experiment involved recording SEPs before and after the subjects performed a repetitive thumb abduction task for 20 minutes. The results suggest that the cortical system becomes less able to suppress the dual input after 20 minutes of repetitive thumb abduction.[22] These SEP changes were unrelated to peripheral factors, as the N9 responses remained stable. The N9 SEP peak reflects the afferent signal over the brachial plexus[27] before it enters the CNS, and thus can be used to ensure that the incoming signal is consistent before and after an intervention. Furthermore, these experiments demonstrated that the subjects' N30 SEP peak ratios decreased significantly after a single chiropractic manipulation of the cervical spine. As the N30 SEP peak is thought to reflect early cortical SMI,[28] the authors argued that their results suggest that the subject's SMI networks' ability to suppress the dual input after the adjustment was increased.[14] The N30 SEP peak ratios remained decreased even after repeating the 20-minute repetitive thumb abduction task. This suggested that the treatment effects appear to have altered the way in which each subject's CNS responded to the repetitive thumb typing task.[14]

Using dual somatosensory input and comparing the SEP ratios are more robust against the variations in placement of recording and stimulating electrodes that can affect SEP amplitudes when measuring SEP data evoked from stimulation of a single peripheral nerve. As it measures the degree of central surround-like inhibition of somatosensory input, it is less affected by the recording and stimulating setup, thus allowing more reliable measures over time and enabling us to compare across subjects. Thus, it may be a useful tool to measure long-term central neurophysiological changes that may occur with chiropractic care.

The purpose of this preliminary study was to assess whether the dual SEP technique is sensitive enough to measure changes in cortical intrinsic inhibitory interactions in patients with chronic neck pain after a 12-week period of chiropractic care and, if so, whether any such changes related to changes in symptomatology.

Methods

Subjects

Six subjects (1 woman and 5 men), aged 24 to 50 (mean age, 36.2 ± 12.8 years) with a history of chronic recurring neck or upper limb symptoms (ie, >3 months in duration and severe enough for the subject to have sought previous treatment for this symptom). The upper limb symptoms were assessed according to the Southampton examination schedule for the diagnosis of musculoskeletal disorders of the upper limb,[29] which has been reported to have good interperson reliability.[30]Inclusion criteria were age 18 through 50 years and a history of pain longer than 3 months. Subjects were excluded if they had a history of neurologic disorders such as epilepsy, multiple sclerosis, dystonia, and abnormal peripheral nerve function. Subjects were recruited from acquaintances of staff and students at the New Zealand College of Chiropractic and University of Auckland through word of mouth during the period from December 2006 to December 2007. Five of the subjects were deemed to be right-handed (mean laterality quotient, 75.5%; range, 64.7%-85.7%) and one left-handed (laterality quotient, 66.0%), using the Edinburgh handedness questionnaire.[31]

All subjects were screened for possible contraindications to treatment or the presence of diseases or disorders that may require medical management (eg, history of previous fractures; high blood pressure; and metabolic, inflammatory, or neoplastic disease). Subjects were also excluded if they had less than 3 months of neck or upper limb symptoms (or both), had received treatment for this condition, or had been prescribed pain medication within the previous 6 weeks. All screening examinations and assessment sessions were conducted by a chiropractor. Written informed consent was obtained from all participants by the same chiropractor (H.H.), and the local ethics

Table 1. *Participant Demographics, Subjective Complaint Area and Duration Prior to Study Participation, and Diagnosis Given* [a]

Subject No.	Sex	Age at Time of Study	% Right Handed	Complaint	Duration	Diagnosis Given
1	F	50	34.00	Neck pain and bilateral elbow pain (left worst)	8 y	Chronic neck pain and bilateral lateral epicondylitis
2	M	49	64.70	Right elbow, forearm, left elbow pain	7 y	Neck stiffness and tension, bilateral lateral epicondylitis, and nonspecific diffuse right forearm pain
3	M	20	85.70	Neck pain (whiplash 5+ y ago)	5 y	Chronic neck pain following whiplash
4	M	24	66.67	Left shoulder pain	2 y	Left rotator cuff tendonitis
5	M	32	83.30	Left arm and neck pain	3 y	Chronic neck pain and left nonspecific diffuse forearm pain
6	M	42	85.70	Right forearm pain (including carpal tunnel)	4 y	Right nonspecific diffuse forearm pain and carpal tunnel syndrome

F, female; *M,* male; *y,* year.

[a] Upper limb symptoms were assessed according to the Southampton examination schedule for the diagnosis of musculoskeletal disorders of the upper limb and diagnosed according to their diagnostic criteria.[29]

committee approved the study (Northern Y Regional Ethics Committee Reference: NTY/07/05/054). Participant demographics and their reported symptomatic area and diagnosis given are summarized in Table 1.

SEP Stimulating and Recording Parameters

The stimulating electrodes (cathode proximal) were placed over the median and ulnar nerves at the wrist of the symptomatic arm. If no arm was symptomatic (ie, the subject had only neck pain), the dominant arm was used for SEP stimulation. If both upper limbs were symptomatic, recordings of both arms were obtained (this was the case for 2 subjects). Stimuli (at 1× motor threshold) consisted of electrical square pulses of 1-ms duration delivered at a rate of 2.47 Hz, a rate that does not lead to SEP peak attenuation,[32] through 7-mm Ag/AgCl disposable, adhesive electrodes (Hydrospot from Physiometrix) (impedance, <5 kΩ). Motor threshold was defined as the lowest intensity that produced a visible muscle contraction of the abductor pollicis brevis muscle for median nerve stimulation or abductor digiti minimi muscle for ulnar nerve stimulation.

All SEP recording electrodes were placed according to the International Federation of Clinical Neurophysiologists recommendations.[27] Recording electrodes were placed on the ipsilateral Erb's point (on the side of the neck 2 to 3 cm above the midpoint of the clavicle and in front of the transverse process of the sixth cervical vertebra), over the C6 spinous process (Cv6), and 2 cm posterior to contralateral central and frontal scalp sites C3/4 and F3/4, which will be referred to as Cc′ and Fc′, respectively. Cc′ and Fc′ recording electrodes were referenced to the contralateral earlobe. The C6 spinous electrode was referenced to the anterior neck (tracheal cartilage). The Erb's point electrode was referenced to the contralateral shoulder. Finally, the central Cc′ electrode was also referenced to the contralateral shoulder (ie, at the midpoint of the spine of the scapula) as SEP components originating from subcortical regions are best recorded with a non-cephalic reference.[33] A ground electrode was attached to Fz. During the data recording sessions, the subjects were installed in a quiet room and seated in a reclining La-Z-Boy chair. Throughout the course of the experiment, subjects were asked to sit still and be as quiet as possible. During the SEP recordings, the lights in the room were also turned off, and subjects' eyes were closed. Ambient light was still able to enter the room, so the room was not completely dark during the recording sessions. Figure 1 depicts the placement of the stimulating and recording electrodes used in this study.

Experimental Protocol

The subjects were asked to attend 3 measurement sessions to record data. A baseline session was followed by a 2-week control period with no intervention, after which there was a postcontrol recording session. The subjects then received 12 weeks of chiropractic care, which was followed by a third recording session. At each session, 3 SEP trials were carried out in a randomized order from 1 or both upper limbs: 1 trial following stimulation of the median nerve individually (M), 1 following stimulation of the ulnar nerve individually (U), and 1 following simultaneous stimulation of both nerves (MU). Before and after the 12 weeks of chiropractic care, subjects were also asked to rate their current pain and their average pain over the last week using a 100-mm visual analog scale (VAS).[34]

Interventions

The 2-week control period, during which no intervention was applied, was followed by a 12-week chiropractic care intervention. During the 12 weeks of chiropractic care, the chiropractor assessed and treated the subject as she would any other chronic pain patient. The participating chiropractor (H.H., with 7 years clinical experience) assessed the spine for segmental dysfunction using tenderness on

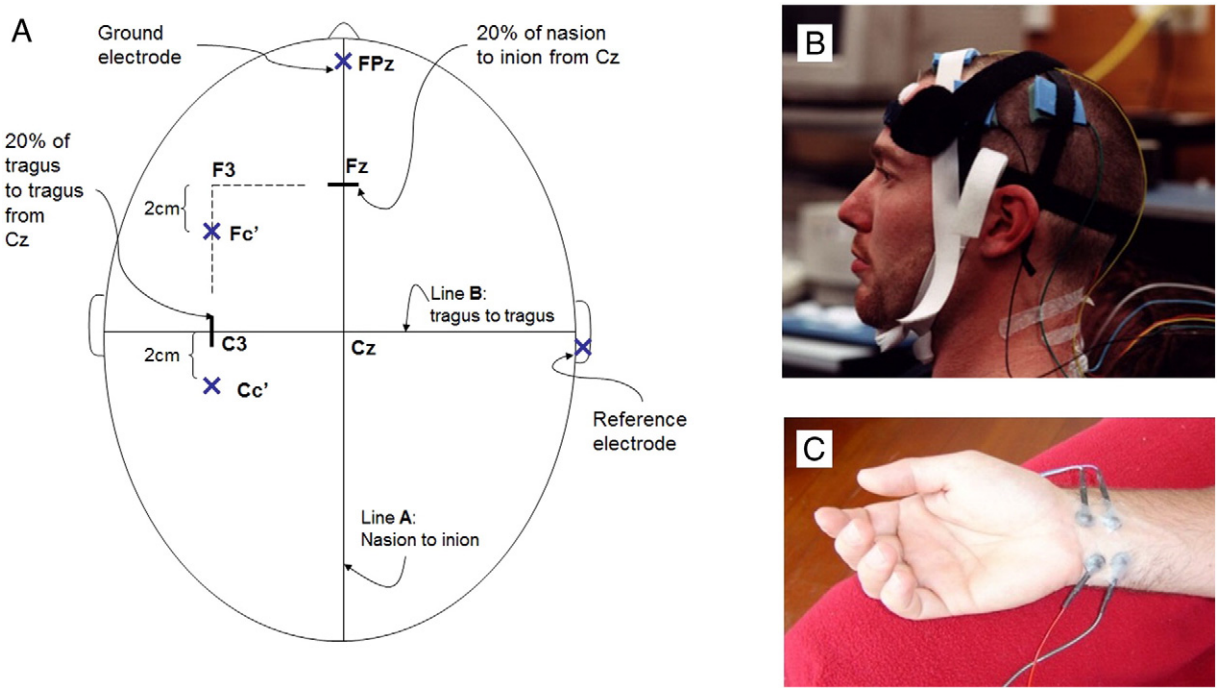

Fig 1. *A, Electrode placement viewed from above. B, Lateral view of electrode placement and attachment on a model's head and neck. C, Placement of the median and ulnar nerve-stimulating electrodes.*

palpation[35-37] and passive intervertebral and global motion of the spine.[38-41] Other treatments included as part of chiropractic care were exercises, peripheral joint adjustments/manipulations, soft tissue therapy, and pain education if deemed by the chiropractor to be appropriate based on history and examination. The chiropractic adjustment/manipulation was the delivery of a high-velocity, low-amplitude thrust to dysfunctional spinal segments.[14]

The chiropractic care plan was pragmatic and generally consisted of 2 to 3 visits per week for the first 2 to 3 weeks. Frequency was reduced based on clinical findings and patient symptomatology. By the end of the 12-week period, participants were seen once or twice a week. No requirements were placed on the treating chiropractor, other than including chiropractic adjustment or manipulation during treatment; thus, the care plan was designed in conjunction with patient preferences and was based on the patients' history, symptoms, wishes, and time availability as well as the clinician's clinical experience and knowledge.

Data Collection and Analysis

The signals were bandpass filtered (3-1000 Hz, –6-dB octave rolloff), amplified (gain 100 000) and then passed to a National Instruments Data Acquisition Board (NI-AT-MIO-46E-3) via a specially shielded cable and National Instruments Cable box (SC2056; National Instruments, Austin, TX). LabView 7 (National Instruments), a commercial software package, was used to control the NI-AT-MIO-46E-3 board. The LabView program controlled the data acquisition, signal averaging, and graphing functions for data analyses. Electroencephalography recordings were digitized at a sample rate of 5000 samples per second and recorded with a sweep length of 55 ms (5 ms prestimulus and 50 ms poststimulus). A total of 1000 sweeps were averaged and displayed on an analysis panel from which the waveforms of interest were measured for amplitude and latency. Only trials with a stable peripheral nerve volley (N9 peak amplitude) were included for analysis. This was achieved by including trials for analysis only if the N9 SEP peak amplitude was within ±10% of baseline values and the N9 MU to M + U ratio was within the range of 0.92 to 1.08. At motor threshold stimulation, the SEP ratio (MU to M + U) calculated for the N9 SEP peak amplitude, which is recorded over Erb's point, should equal 1 to indicate that no suppression of the electrical signal is occurring at the peripheral level (ie, at the brachial plexus).

Prior to any SEP peak analysis, the data files were coded by an independent person to reduce any bias during SEP peak amplitude and latency analysis. SEP amplitudes were measured, from the averaged (800 sweeps) nonrectified traces, from the peak of interest to the preceding or succeeding peak of opposite deflection, according to international recommendations[27] and past studies in this field.[42-45] SEP latencies were measured at the peak of the waveform of interest. The amplitude and latency of the peripheral N9, spinal N11 and N13, far-field P14 and N18

Table 2. *Mean Raw Amplitude and Standard Deviation (SD) of Simultaneous (MU) and Summed (M + U) Median and Ulnar Nerve SEPs for Recordings at Baseline, After the 2-Week Control Period, and After 12 Weeks of Chiropractic Care*

	N9 (μV)			N13 (μV)			P14-N18 (μV)			N20-P25 (μV)			P22-N30 (μV)		
	MU	M + U	MU/ (M + U)	MU	M + U	MU/ (M + U)	MU	M + U	MU/ (M + U)	MU	M + U	MU/ (M + U)	MU	M + U	MU/ (M + U)
Baseline	3.58	3.52	1.05	3.05	3.85	0.96	2.49	3.50	0.75	5.25	6.94	0.77	2.56	3.31	0.78
SD	2.49	2.61	0.13	1.74	1.74	0.84	0.97	1.57	0.20	1.79	2.76	0.14	2.09	2.27	0.17
After control period	2.82	3.31	0.95	3.15	4.85	0.70	2.37	3.52	0.75	5.44	7.77	0.73	2.89	3.45	0.86
SD	0.45	1.10	0.06	1.28	1.94	0.29	0.97	1.36	0.35	1.30	2.60	0.13	1.32	1.80	0.17
After chiropractic	3.08	2.97	1.05	2.88	3.77	0.80	2.38	3.08	0.76	5.75	6.73	0.87	2.10 [a]	4.41	0.52 [b]
SD	1.85	1.99	0.09	1.33	1.78	0.29	1.50	1.06	0.31	1.46	1.74	0.16	1.82	3.77	0.22

[a] $P < .05$ compared with baseline values.
[b] $P < .001$ compared with baseline values.

potentials, parietal N20 (N20-P25 complex), and frontal N30 (P22-N30 complex) were identified and measured. This was done for the individual median (M) and ulnar (U) nerve recordings, the simultaneous median and ulnar (MU) recordings, and the traces derived from the arithmetic sum of the individual M and U recordings. Finally, the MU to M + U SEP peak ratios were calculated. This was achieved by dividing the amplitudes of the SEP peaks obtained by stimulating the median and ulnar nerves simultaneously (MU) by the amplitude value calculated as the arithmetic sum of the SEPs elicited by stimulating the same nerves separately (M + U). After all SEP peak amplitudes and latencies had been measured from the M, U, and M + U traces, the data were decoded, grouped according to intervention, and transferred into SPSS statistical software (Version 22 for Windows, IBM, Armonk, NY) for statistical analysis.

Tests of normality were performed and then repeated-measures analysis of variance (ANOVA) tests were run with the averaged M amp, U amp, MU amp, M + U amp, and MU to M + U ratio data for each SEP component as dependent variables and time (baseline, after 2 weeks [no intervention], after 12 weeks [of intervention]) as the independent variable. If significance was observed, post hoc paired *t* tests were performed using the Bonferroni correction to investigate whether mean differences occurred during the control or experimental period. The level of significance was set at $P < .05$.

Visual analog pain scale data, both current and pain last week, were analyzed using paired *t* tests, and then changes in pain scale scores were compared with changes in significant SEP data using the Pearson correlation coefficient. The sample size was determined using a power calculation based on previous work conducted in our lab and allowed us to detect an effect size of 0.8 with power set to 0.8 and an α of 0.05.[15]

Results

All subjects completed the trial and there were no missing data. All subjects conformed to the care plan and no adverse events were reported. The averaged baseline recordings elicited from the simultaneous stimulation of the median and ulnar nerves produced SEPs for which the amplitudes of the central SEP complexes (ie, N13, P14-N18, N20-P25, and P22-N30) were, for the most part, smaller than the amplitudes of the arithmetic sums of the individual median and ulnar SEPs (see Table 2 for grand averages). However, for some individual subjects, their simultaneous median and ulnar nerve elicited central SEP amplitudes larger than the amplitude of the arithmetic sum of the individual SEPs (see Fig 2 for an image of the N30 SEP complex).

Somatosensory evoked potential peak amplitudes and latencies, as well as the averaged MU and M + U data, were relatively normally distributed according to Shapiro-Wilk tests of normality. There were no significant changes in any of the N13, N18, or N20 SEP peak measures ($P > .05$). Neither the N30 M or U individual SEP peak changed over the course of the study; however, there was a significant difference in the N30 MU amp ($F[2, 14] = 4.51$, $P = .031$) and N30 MU to M + U ratio data ($F[2, 14] = 13.96$, $P < .001$). Post hoc tests using the Bonferroni correction revealed significant mean differences in N30 MU amp ($P = .049$) and N30 MU to M + U ratio data ($P = .001$) during the chiropractic intervention, but no significant changes were observed during the control period ($P = .1$ for N30 MU amp and $P = .3$ for N30 MU to M + U ratio data). The effect size for the change in N30 MU amp was 0.61, and for the N30 MU to M + U ratio it was 0.66. The N30 ratio change represented on average a 37.4% decrease following the 12 weeks of chiropractic care (Fig 3). The N30 MU amplitude change following chiropractic care represented an 18.0% decrease in amplitude compared with baseline (Figs 4 and 5). No other significant changes were observed.

Figure 2 illustrates, in one representative subject, the changes in the difference between the MU and M + U traces for the P22-N30 SEP amplitudes before and after the 2-week control condition and before and after 12 weeks of chiropractic care. Note that the MU traces at baseline and after 2 weeks of control are larger than the M + U amplitudes for this particular subject, and after 12 weeks of chiropractic care, this is reversed. This represents a decrease in the MU to M + U SEP ratio for the P22-N30 SEP complex following chiropractic care.

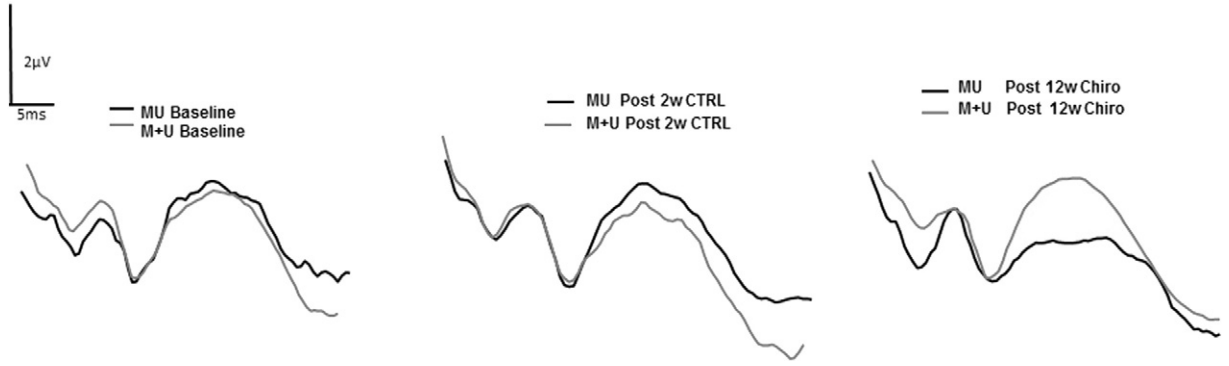

Fig 2. *Representative set of preintervention SEP peaks (first set of traces) at baseline, after the 2-week control period (middle set of traces), and after 12 weeks of chiropractic care (third set of traces) recorded in a single subject. Note the precentral (Fc′) SEP peaks from both the median and ulnar (MU, black traces) and median + ulnar (M + U gray traces) trials (1000 sweeps each).*

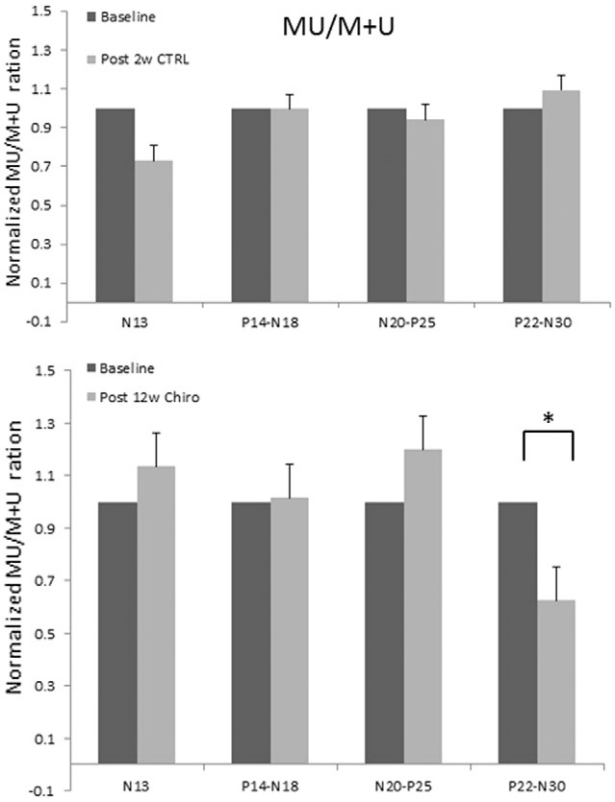

Fig 3. *Bar graphs of averaged normalized SEP ratios (median and ulnar to median + ulnar, ± SE) before and after the control intervention (top) and before and after the cervical manipulation intervention (bottom). The frontal P22-N30 peak ratio is significantly reduced after 12 weeks of chiropractic care and is marked with a star. This decrease in SEP ratio represents an increase in inhibition of the dual input from the 2 peripheral nerves occurring at the cortical level.*

No significant changes were observed for any of the individual M or U SEP peak amplitudes after either control or chiropractic interventions (Table 3). There were no significant changes for the M + U data for any SEP peak after the chiropractic intervention (Table 2 and Fig 4).

Both the patient's current pain and the pain from the last week decreased significantly while the subjects were receiving chiropractic care (Fig 6). On average, pain dropped from 4.1 to 1.8 on the VAS (P = .02) and pain last week dropped from 6.4 to 4.5 (P = .01). The correlation between MU change and changes in current pain (r = –0.04) or pain last week (r = –0.26) were weak. Moderate nonsignificant positive correlations were observed in both changes in current pain (r = 0.62) and changes in pain last week (r = 0.51) when compared with changes in MU to M + U ratio.

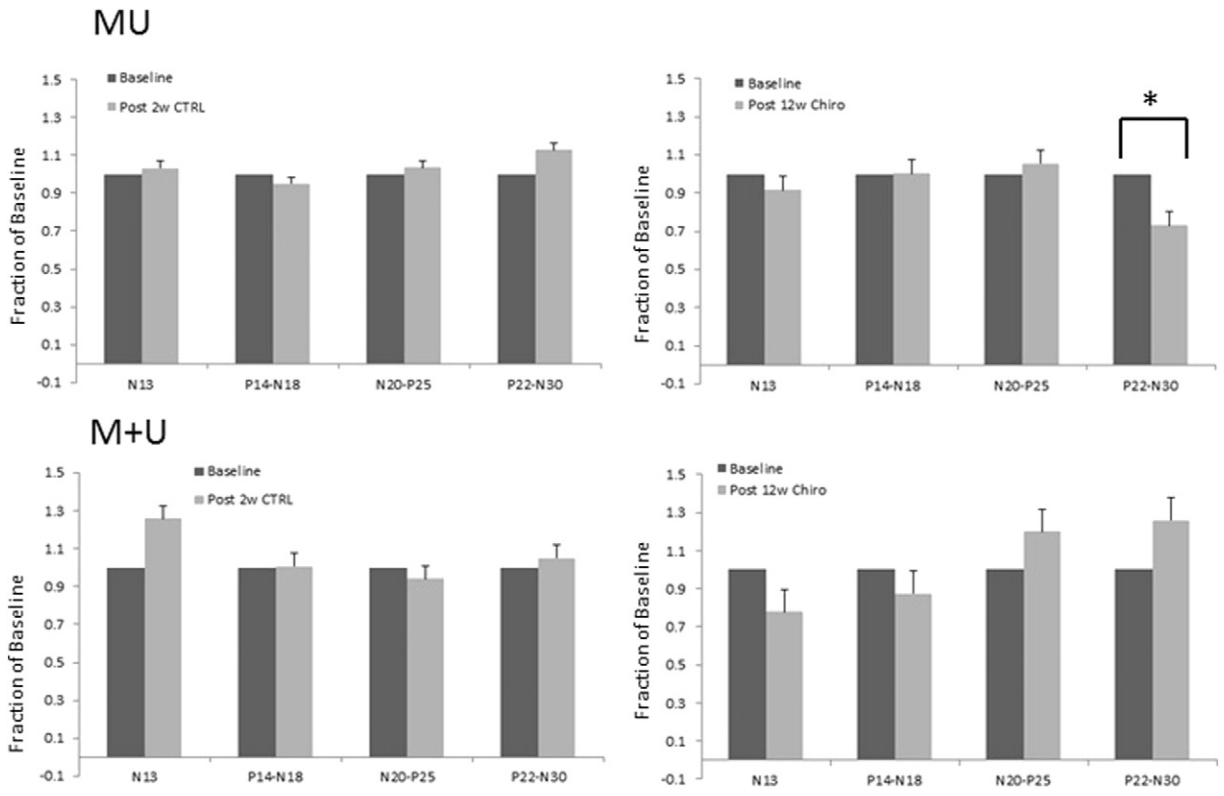

Fig 4. *Bar graphs of averaged normalized SEP peak median and ulnar (MU, top) and median + ulnar (M + U, bottom) data ± SE before and after the 2-week control period (left) and before and after 12 weeks of chiropractic care values (right). Note that the frontal P22 -N30 normalized MU amplitude was significantly decreased after the 12 weeks of chiropractic care and is marked with a star.*

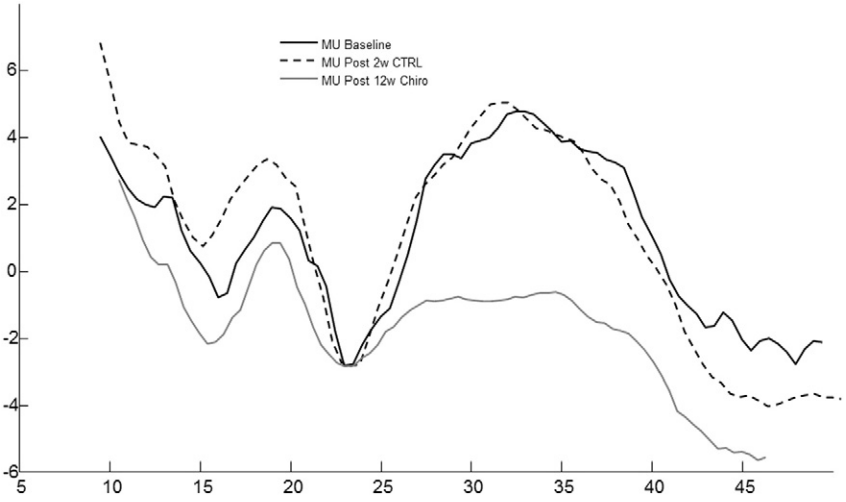

Fig 5. *Representative set of precentral (Fc') median and ulnar (MU) somatosensory evoked potential (SEP) traces in one subject at baseline, after the 2-week control period, and after 12 weeks of chiropractic care have been superimposed. Note the decrease in the frontal P22-N30 SEP peak MU amplitude after chiropractic care.*

Discussion

The major finding in this preliminary study was that after 12 weeks of chiropractic care in a small sample of chronic pain patients, there was evidence of improved suppression of SEPs evoked by dual-upper-limb nerve stimulation at the cortical level of the lemniscal pathway. More specifically, the improved suppression of dual input was evident for the frontal P22-N30 SEP component. Alongside this change in the N30 SEP ratio, the subjects reported a decrease in both

Table 3. *Mean Raw Amplitude and Latency Data With Standard Deviations of Individual Median and Ulnar Somatosensory Evoked Potential Components for Recordings at Baseline, After the 2-Week Control Period, and After 12 Weeks of Chiropractic Care*

	N13		N18		N20		N30	
	Median	Ulnar	Median	Ulnar	Median	Ulnar	Median	Ulnar
Baseline								
Amplitude (μV)	2.20	1.66	1.92	1.58	3.98	2.96	1.95	1.36
SD	0.92	1.28	0.81	1.00	1.30	1.88	1.39	1.01
Latency (ms)	13.04	13.56	18.10	18.32	18.67	18.89	29.82	29.94
SD	1.01	0.80	1.00	1.50	1.10	1.29	1.46	0.90
After control period								
Amplitude (μV)	2.75	2.10	2.00	1.53	4.63	3.13	2.34	1.11
SD	1.42	1.03	0.92	0.73	1.04	1.89	1.54	0.38
Latency (ms)	13.37	13.46	17.65	18.17	18.84	19.24	29.67	29.85
SD	0.88	0.35	1.10	0.60	1.11	1.07	1.27	0.84
After chiropractic								
Amplitude (μV)	2.01	1.77	1.70	1.38	4.07	2.66	2.23	2.19
SD	0.81	1.00	0.71	0.49	0.99	1.11	1.80	2.04
Latency (ms)	13.09	13.70	17.75	18.34	18.84	19.29	29.64	29.82
SD	0.86	0.90	0.68	0.63	1.08	0.96	0.74	1.15

SD, standard deviation.

current pain and average pain over the last week. A control period of 2 weeks of no intervention resulted in no significant changes in any SEP peak ratio.

Frontal P22-N30 SEP Peak Changes

The changes observed in the current study occurred only for the frontal N30 component of the SEP peaks. Although some authors have suggested this peak is generated in the postcentral cortical regions (ie, S1),[46,47] the majority of the evidence suggests that this peak is related to a complex cortical and subcortical loop linking the basal ganglia, thalamus, premotor areas, and primary motor cortex.[48-52] The frontal N30 peak is therefore thought to reflect SMI.[28] The decreased frontal N30 SEP peak ratio observed in the current study therefore suggests that an increase in surround inhibition or filtering of sensory information from the upper limb may be occurring somewhere in these cortical and subcortical loops linking the basal ganglia, thalamus, premotor areas, and primary motor cortex after 12 weeks of chiropractic care. The SEP ratio change after the chiropractic intervention appears to be caused by an increased inhibition of the dual peripheral input, as the N30 MU data were also significantly decreased. Impaired surround inhibition prior to the period of chiropractic care may account for this finding, and may be an important central neural dysfunction present in chronic pain populations. This should be investigated further. The effect size of the changes in N30 MU amp (0.61) and MU to M + U ratio (0.66) are considered to be moderate and can be used to inform future research.[53]

No changes in MU, M + U, or MU to M + U ratios were observed after the 2-week control period. The results after chiropractic care are therefore unlikely a result of time alone. However, the design of our study cannot prove it was the chiropractic treatment that caused these changes. It could be that other factors, such as natural history, led to the improvement in symptoms, and the altered N30 SEP ratios may simply reflect the symptomatic relief. However, we do not think this is the case, because we have previously reported that a single session of chiropractic adjustments alone in a subclinical population also leads to a significant decrease in the N30 SEP peak ratio (ie, decreased MU to M + U ratio).[14,15]

Central Reciprocal Inhibition and Pain Disorders

The changes observed in dual SEP ratios after several weeks of chiropractic care in a chronic pain population suggest that this treatment option may improve gating of peripheral afferent input to the brain, thus improving impaired SMI in cortical motor areas and improving processing of motor programs. Impaired SMI and defective motor programming is known to be present in various chronic pain populations[6-57] and is implicated in the clinical symptomatology.[58] We know from the literature that in normal circumstances, afferent input to the motor system leads to finely tuned activation of neural elements and ultimately results in the correct execution of movement.[23] Multiple experimental and clinical studies have confirmed the importance of sensory feedback to the motor system.[23,59] Thus, distorted sensory information is thought to disturb SMI and impair accurate motor control. In normal circumstances, 2 inputs that engage the sensory system have a reciprocally inhibitory action that gates the total amount of signal at all central levels, spatially and temporally limiting the amount of input engaging the CNS. This is thought to prevent sensory "overflow." The defective gating may cause an input-output mismatch in specific motor programs, and such mismatches in motor programs may in themselves lead to production of distorted sensory information and issue of less than ideal motor commands. In this way, the chronicity of the problem can be maintained via a self-perpetuating mechanism. The

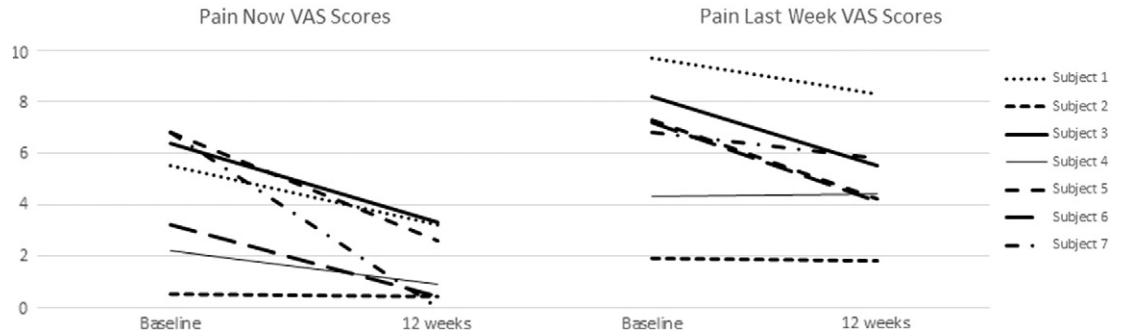

Fig 6. *Visual analog scale (VAS) scores for current pain (left) and average pain last week (right) before and after the 12 weeks of chiropractic care.*

reduced frontal N30 SEP peak ratio observed in the current study after 12 weeks of chiropractic care may reflect a normalization of pain-induced central maladaptive plastic changes and may reflect one mechanism for the improvement of functional ability reported following chiropractic adjustment or manipulation.

Other than pain, additional sensory symptoms are also frequently found in many chronic pain groups,[60,61] and sensory manipulation has been reported to modify clinical severity.[62,63] Interestingly, one of the subjects in the current study complained that his arms felt like "Popeye" arms, as they felt larger and heavier than he knew they were. As the 12 weeks of chiropractic care progressed, this subject reported to one of the examiners that he no longer experienced his arms as "Popeye" arms and that they no longer felt heavy or abnormally large. Several of this subject's central SEP peak ratios were greater than 1 at both baseline and after the 2-week control period. This was the case for his N13 and N30 complexes at baseline and for his N13, N18, and N30 SEP complexes after the 2-week control period. Figure 1 illustrates what this looks like for his N30 SEP complex, where the MU trace is actually larger in amplitude compared with his M + U traces. After the 12 weeks of chiropractic care, when he was also feeling better symptomatically, this was reversed, and all of his MU traces for all SEP peak complexes were smaller in amplitude than his M + U trace, indicating a greater level of central reciprocal inhibition was occurring.

Although the functional importance of this gating is not fully understood, it is thought to play an important role in maintaining an accurate inner body schema, by preserving the spatial separation of the 2 stimuli.[16] Reciprocal sensory inhibition would enhance the contrast between stimuli, so that information from adjacent body parts is perceived and, more importantly, processed separately. Thus, if sensory "overflow" occurs, then incomplete processing of this incoming signal may occur in the brain, resulting in its perceiving not only excessive, but also spatially distorted information. This may have been why our subject felt as if he had "Popeye arms," although he knew this not to be real.

Central Reciprocal Inhibition and Neurological Disorders

As mentioned, conditions such as dystonia[16] and Huntington's disease[23] are known to have increased dual SEP ratios. The increased SEP ratios that have previously been observed for those with dystonia[16] and Huntington's disease[23] suggest that these individuals receive distorted and excessive (ie, not spatially filtered) afferent input from their affected limbs, which may potentially cause their motor system to transform these afferent inputs into abnormal "unhealthy" motor outputs. The chronic pain subjects in our study with increased central SEP ratios may also have been receiving excessive afferent input affecting their upper limb SMI and motor control. The individual whose traces are depicted in Figure 1 was a piano player, and his chronic neck and arm pain could be considered a form of chronic overuse injury, similar in some respects to some types of dystonia. Regardless, this subject exhibited impaired afferent-input gating, as has previously been shown with dystonia that reversed to a more healthy-looking gated signal after 12 weeks of chiropractic care. The results of our study therefore suggest it is worth investigating whether chiropractic care is beneficial for individuals with other neurological conditions that are associated with abnormal central somatosensory gating.

Limitations and Future Studies

This study was not designed to test the efficacy of chiropractic care for treating chronic pain; therefore, conclusions about efficacy cannot be drawn from our findings. The study did not include randomization with an adequate control group, thus limiting the interpretations that can be made about the changes in pain observed in the trial. Causation cannot be claimed. The patients were heterogenous with varying types and degrees of upper limb and cervical pain. Although the reductions in current pain (2.3) and pain from the previous week (1.9) exceeded the values for a minimum clinically important difference for nonspecific neck

pain (0.8), they were not considered to reflect a substantial clinical benefit (2.7) when measured using a VAS.[64] It is also important to note that one of the researchers was also the treating chiropractor, which may have had an effect on patient response.

It is imperative that future large studies explore the relationship between pain changes and cortical intrinsic inhibition further before any firm conclusions can be made. On average, pain now dropped from 4.1 to 1.8 on the VAS ($P = .02$), and pain last week dropped from 6.4 to 4.5 ($P = .01$). The control period was not matched to the period of chiropractic care; thus, changes in dual SEP ratios may occur after 12 weeks, even without chiropractic care. It is also possible that the nonsignificant positive correlations observed between pain levels and N30 MU to M + U ratio ($r = 0.62$ and $r = 0.51$) were not significant because of the small sample size. There was an imbalance between sexes in subject numbers so interactions between sex and the primary outcome cannot be ruled out. Follow-up in larger samples with and without pain would also be valuable in confirming whether larger cortical ratios are truly associated with chronic pain and lower cortical ratios reflect reduced symptomatology.

Conclusion

The P22-N30 complex dual SEP ratio appears to be a measure that could be used alongside clinical measures in future clinical trials to document neurophysiological changes that accompany treatment of chronic pain. The observations of the 6 subjects in the present study suggest that 12 weeks of chiropractic care may improve suppression of SEPs evoked by dual-upper-limb nerve stimulation at the levels of the motor cortex, premotor areas, and/or subcortical areas such as basal ganglia and thalamus. It is possible these findings reflect reduced cortical processing caused by increased gating of excessive sensory information due to the 12 weeks of chiropractic care, and that this may be one of the mechanisms by which chiropractic care improves function and reduces pain for chronic pain patients. However, further studies are needed to elucidate the role and mechanisms of these cortical changes, confirm causality, and confirm their relationship to chronic pain patients' clinical presentation and ability to perform daily tasks.

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Contributorship Information

Concept development (provided idea for the research): H.H., B.M.
Design (planned the methods to generate the results): H.H., B.M., K.H., I.K.N.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): H.H., B.M.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): H.H.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): H.H., I.K.N.
Literature search (performed the literature search): H.H., K.H.
Writing (responsible for writing a substantive part of the manuscript): H.H., K.H.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): H.H., B.M., K.H., I.K.N.

Practical Application

- The results of this study suggest that 12 weeks of chiropractic care may improve gating of peripheral afferent input to the brain, thus improving impaired SMI in cortical motor areas and improving processing of motor programs.
- A few of the chronic pain patients in this study exhibited abnormal gating of proprioceptive afferent input prior to chiropractic care (their medial and ulnar N30 amplitudes were larger than their medial + ulnar amplitudes), which were reversed after the 12 weeks of chiropractic care (noting that the current study design cannot prove causation).
- The P22-N30 complex dual SEP ratio appears to be a measure that could be used alongside clinical measures in future clinical trials to document neurophysiological changes that accompany treatment of chronic pain.
- This study supports previous research that suggests that altered sensory processing and motor control may be implicated in the development of chronic neck pain.

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