

Vibro-tactile stimulation as a non-invasive neuromodulation therapy for
cervical dystonia: a case study

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Yi Zhu

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Advisor: William Durfee

Co-advisor: Jürgen Konczak

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Dedication

This dissertation is dedicated to the memory of my grandma Wang. She was my inspiration to pursue my M.S. degree in Biomedical Engineering, a major that could help people live a better life. Unfortunately, she was unable to see my graduation. This is for her.

I also dedicate this dissertation to my family who have supported me throughout the process. I will always appreciate all they have done.

Abstract

Background: Cervical dystonia (CD) is a type of focal dystonia characterized by involuntary neck postures. The underlying neurophysiology mechanism of CD is unknown, but it has been long hypothesized to be associated with somatosensory and proprioceptive deficits. As a form of somatosensory stimulation approach, vibro-tactile stimulation (VTS) is known to alter afferent signals from the vibrated mechanoreceptors in muscles and tactile receptors in the skin. Previous studies have shown that VTS can be an effective neuromodulation therapy for treating laryngeal dystonia. **Objectives:** This proof-of-concept study examined the effect of VTS on alleviating the involuntary cervical muscle contractions in two adolescents with different presentations of CD – a male with consistent retrocollis and a female intermittent torticollis. **Method:** VTS was applied sequentially on four neck positions: bilateral trapezius (TRP) and bilateral sternocleidomastoid (SCM). Each VTS site was vibrated continuously for six minutes. The kinematics and underlying neck muscle activities during dystonic neck movements were examined with acceleration and surface electromyography (sEMG). Two acceleration features and two sEMG features were derived: (1) number of peaks per minute; (2) peak amplitude of acceleration (PAA); (3) change in power of sEMG after VTS; (4) cumulative density function of sEMG between 3-10 Hz (CDF₁₀). **Results:** First, the application of neck muscle VTS did not induce meaningful symptom relief for the participant with constant retrocollis. Second, the frequency of dystonic neck movements decreased by 60% after VTS in the participant who presented with intermittent torticollis. In addition, PAA during dystonic episodes was significantly lower in post VTS when compared to baseline. Third, the effectiveness of VTS in alleviating dystonic muscle spasms depended on the site of vibration. For the patient with right torticollis, the left trapezius muscle was the optimal vibration site reducing sEMG signal power by 15% across all recorded muscles. During VTS on the optimal vibration site, sEMG power of left trapezius dropped rapidly within the first minute and then continued to decline over time. As an additional result, the mean CDF₁₀ of left trapezius in post VTS condition was found significantly lower than baseline. **Discussion:** This case study offered preliminary insight into the assumed effectiveness of neck muscle VTS as a treatment for CD. One participant responded positively to VTS. The frequency and extent of the dystonic postures were markedly reduced during and immediately after VTS application. A

systematic study with larger sample size is required in the future to validate the effectiveness of VTS for treating symptoms in CD.

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Other (list of abv.)

Cases

BoNT: botulinum neurotoxin	5
CD: Cervical Dystonia	1
CDF: cumulative density function	2
sEMG: surface electromyography.....	2
SCM: sternocleidomastoid.....	1
TRP: trapezius.....	1
VTS: vibro-tactile stimulation	6

Chapter 1: Introduction

1.1 Definition and clinical symptoms of Cervical Dystonia

Cervical dystonia (CD) is a type of focal dystonia characterized by involuntary neck muscle contractions, resulting in abnormal cervical movements or postures (Tijssen et al., 2000a). CD is the most common form of focal dystonia with a prevalence of 20 to 4100 cases per million (Defazio et al., 2013). Most prominent symptoms observed in CD are: 1) involuntary contractions in neck muscles, which lead to sustained or intermittent head turnings; 2) pain; 3) neck muscle stiffness (Chan et al., 1991).

The pattern of dystonic neck movement and postures is variable in patients with CD. Symptoms are clinically categorized into torticollis, laterocollis, retrocollis, or anterocollis (Stacy, 2008). Torticollis is the most common form of CD, where the head remains upright and may turn to one side intermittently then releases. Laterocollis is the second most common form of CD, where the head is pulled laterally to one side of the shoulder. Retrocollis and anterocollis happen respectively when the head is pulled backwards (head extension) and towards the chest (head flexion). It is reported that 83% of the individuals with CD have constant (vs. intermittent) head deviations in more than 75% of the time when sitting with their head unsupported (at rest). Instead of single-plane movement, head deviations always occur as multiplanar movement. For individuals with complex head turnings or referred to as rotating torticollis, 81% also had neck tilting in variations (Chan et al., 1991). Individuals with CD may also have additional signs and symptoms, such as shoulder elevation, neck/shoulder pain, head oscillation due to dystonic tremor produced by uneven contractions of the cervical muscles, arm tremor, and use sensory tricks (Defazio et al., 2013).

Previous studies investigated cervical muscle groups that are activated during dystonic movement in individuals with CD (De Menezes and Rho, 2002a). Results showed that rotating torticollis is due to dystonic activity of ipsilateral splenius capitis (SPL) and/or contralateral sternocleidomastoid (SCM) (Deuschl et al., 1992). One-third of the patients had also dystonic muscle activation of the contralateral SPL, and rarely of the contralateral trapezius (TRP) (Deuschl et al., 1992). Though there has not been golden standard for the identification of dystonic muscles to characterize CD, SPL, SCM, and

TRP are the three muscles that have been commonly studied as principally involved muscles in CD (Chan et al., 1991; Deuschl et al., 1992; Dauer et al., 1998; Tijssen et al., 2000b; De Menezes and Rho, 2002b; Schramm et al., 2017).

1.2 Signatures of CD

1.2.1 Electrophysiological signatures of CD

To investigate electrophysiological signatures behind CD, electromyography (EMG) has been widely used to record dystonic muscles' activation (Gerpen et al., 2000). EMG is an electrodiagnostic technique to record electrical activities produced by motor neurons. As EMG signals tend to change over time, frequency analysis is often used to investigate signal signatures in frequency domain (Gerpen et al., 2000).

Although no uniform electrophysiological feature was concluded as the general feature of the dystonic movement, there has been a hypothesis that a downward shift in the power of EMG signal exists in dystonic compared to non-dystonic muscles (Tijssen et al., 2000b; Nijmeijer et al., 2014, 2017; Bruijn et al., 2017a). In line with the hypothesis, studies have shown that power of EMG between 3-10 Hz in CD patients is higher than healthy individuals during isometric contractions (Nijmeijer et al., 2014). Quantitative signatures of dystonic muscles were most clear and most significant in the cumulative density function of EMG between 3-10 Hz, which was defined as the ratio of power in the lower (3-10 Hz) band to the 3-30 Hz band (Bruijn et al., 2017a). Previous studies have shown increased CDF_{10} values in CD patients, representing higher signal power between 3 and 10 Hz, relative to power between 3 and 30 Hz (Nijmeijer et al., 2017) (Figure 1). Furthermore, with a cut-off value of $CDF_{10} = 0.222$, in an isometric contraction task dystonic muscles in CD patients can be identified from non-dystonic muscles in healthy controls (Nijmeijer et al., 2017). The results indicate that the value of CDF_{10} was higher in dystonic muscles, due to an increase in power for 3-10 Hz and power decrease for 10-30 Hz frequency band.

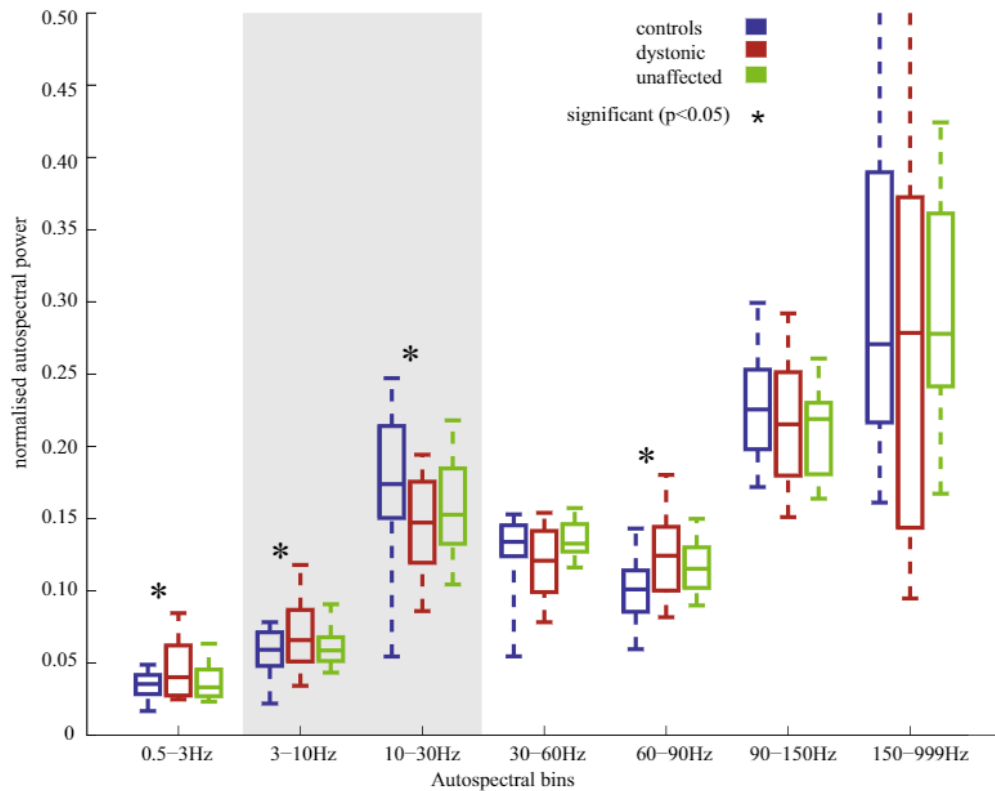


Figure 1. Normalized power of muscles divided into bins. Box plots indicate median, first and third quartile, and dotted lines show a 9–91% point span. The shaded area denotes the 3–30 Hz frequency band. Significant increases in normalized power of the dystonic muscles compared to controls are seen at low frequencies and in the 3-10 Hz and 10-30 Hz (shaded area). Figure from (Nijmeijer et al., 2017) with modification.

1.2.2 Kinematic signatures of CD

Compared to healthy individuals, it takes longer time for CD patients to turn their head to the target position, which is defined as a slow saccade and measured by time difference for the patients to reach target location in comparison with healthy controls (Gregori et al., 2008). The velocity of head saccades is normal in CD compared to healthy individuals, but longer duration results from frequent interruptions during the movement (Shaikh et al., 2015) (Figure 2). Results suggested that the head saccade is programmed normally but is unintentionally dispersed into a series of short phases, which leads to an overall longer duration to reach the target.

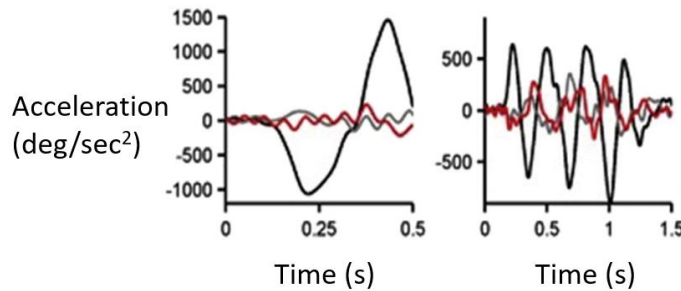


Figure 2. Acceleration of one rapid voluntary goal directed head movement. Healthy control (left). CD patient (right). The black trace depicts horizontal movement, the red trace depicts vertical movement, and the grey trace is torsional movement. Figure from (Shaikh et al., 2015) with modification.

The neurological explanation for this phasic movement is still under discussion, one hypothesis is that the excitement of ipsilateral neck neurons triggers the activation of the agonist muscles, but the same signals also evoke contractions in the antagonist muscles which suppresses the voluntary movement and leads to the interruptions (Shaikh et al., 2015). This hypothesis is consistent with findings in other forms of dystonia that such interruptions in dystonic muscle regions might be caused by activation in antagonist muscles (Kamp et al., 1989; Gregori et al., 2008).

1.3 Neurophysiology of CD

The underlying neurophysiological mechanism of CD is unknown. It has been long hypothesized to be associated with somatosensory and proprioceptive deficits (Grünewald et al., 1997; Kägi et al., 2013). In CD, vibration on neck muscles may induce postural responses such as enhanced control of body sway (Lekhel et al., 1997). Abnormal integration of proprioception is further supported by findings of deficits in kinesthesia when the fingers were passively moved (Putzki et al., 2006). A recent study investigated the effect of botulinum neurotoxin (BoNT) injection on wrist proprioception and corresponding sensorimotor cortical activities in CD patients (Khosravani et al., 2020). During an active movement wrist position matching task, an excessive rise of premotor/motor cortical β -oscillations (13-30Hz) with a significantly larger error in matching wrist position was observed in CD patients when compared to healthy controls. This abnormal active position sense of CD patients is in line with the hypothesis of the proprioceptive dysfunction in CD. Furthermore, this higher cortical activity and error in wrist match task declined after the BoNT injection, indicating that local injections may

affect the central mechanisms of proprioceptive function in CD (Khosravani et al., 2020). Together, these findings point to underlying somatosensory and proprioceptive impairments in CD.

1.4 Current Treatment for CD

BoNT injection is currently the primary treatment for CD. However, it can induce unwanted side effects and is not tolerated well by a sizable group of patients (Jinnah et al., 2016). Sensory trick has been long established to alleviate focal dystonia (Tang et al., 2007; Kägi et al., 2013; Patel et al., 2014; Brugger et al., 2018; Khosravani et al., 2019). The sensory trick usually involves the patient touching his or her chin with the hand that is contralateral to the direction of head turn. It is not simply a counterpressure phenomenon since relaxation of dystonic muscles can precede the actual touch trick (Wissel et al., 1999). For CD, it is known that this sensory trick could alleviate involuntary cervical muscle contractions by touching skin areas around dystonic muscles (Poisson et al., 2012; Kägi et al., 2013; Brugger et al., 2018), which sheds light on the link between underlying somatosensory deficits and abnormal muscle contractions.

Vibro-tactile stimulation (VTS) is a form of somatosensory stimulation is known to alter afferent signals from the vibrated mechanoreceptors in muscles and tactile receptors in the skin (Cordo et al., 1995). VTS was shown to improve voice quality and suppress theta band power in left somatosensory motor cortex in spasmodic dysphonia, as another type of focal dystonia (Khosravani et al., 2019). Results showed that short-term application of VTS over the skin above the larynx, will result in improvement of voice quality and symptom release in 69% of the tested participants who had spasmodic dysphonia (Khosravani et al., 2019).

However, the effect of VTS on CD is not clear. It is known that short-time vibration in the range of 40-100 Hz on the dorsal neck muscles (10-35 s) might induce involuntary movements of the head in patients with CD (Lekhel et al., 1997). The effect of long-time vibration was tested in a single study showing that after a 5-second vibration head position returned to the initial position within seconds, but with prolonged stimulation for 15-minute the head position was corrected and then decreased slowly within minutes to

the initial tilted position (Karnath et al., 2000). Thus, further investigation is needed to explore the comprehensive effect of VTS on CD.

1.5 Purpose and Specific Aims

To address the clinical need of an alternative behavioral therapy for individuals with CD, this proof-of-concept study investigated, if VTS of neck muscles is a suitable non-invasive form of neuromodulation that induces measurable improvements in CD. To this end, this study pursues two aims:

First, to obtain preliminary data on the assumed effectiveness of VTS in reducing the extent and frequency of dystonic head postures in CD.

Second, to examine the dependency of muscle vibration site on reducing dystonic muscle activity.

If successful, the work would lay the scientific foundation for a clinical trial to examine the usefulness of VTS in a larger sample. It would document the preliminary data of how VTS alleviates dystonic neck postures in CD. It would promote the development of wearable, user-programmable medical devices that could apply VTS while monitoring its effect on CD symptoms in real-time. Ultimately, VTS would enlarge the therapeutic arsenal by becoming an alternative intervention option for CD patients.

Chapter 2: Methods

2.1 Study Design

2.1.1 Participants

Two adolescents with CD were recruited, a 12-year-old male and a 10-year-old female. Both participants received regular Botox injections as a symptomatic treatment. They were at the end of their Botox treatment cycle when participating in this study, i.e. they were in their symptomatic stage. Different presentations of CD were observed on the two participants. The male participant reported to have left and right posterior neck muscles diagnosed as dystonic muscles, which led to a sustained neck extension or *retrocollis*. The other participant presented with intermittent right *torticollis* with concurrent left shoulder elevation. Both participants had a certain level of discomfort when dystonic movement/posture occurred.

2.1.2 Apparatus

Surface electromyography (sEMG). To record muscle activity, an sEMG system (Biometrics Ltd.) was used for this study. Four sEMG electrodes were respectively attached to bilateral sternocleidomastoid and trapezius muscles to record electrical activity. One ground electrode was attached to C7 spinal segment (Figure 3). The sEMG amplifier (Biometrics Ltd., Model SX230FW) has two flying wire leads for use with any reusable or disposable sEMG electrode incorporating a 4mm snap (Figure 4A). The maximum inter-electrode distance is 170mm and the minimum distance is dependent upon the size of the electrodes used. A sEMG datalogger (Biometrics Ltd., Model DataLOG MWX8) is used to portably collect data (Figure 4B).

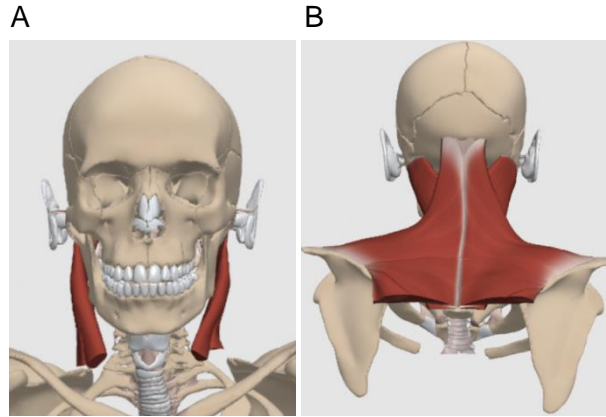


Figure 3. Placement of sEMG electrodes on cervical muscles. (A) left and right sternocleidomastoid. (B) left and right trapezius. Blue markers show the placement of electrodes.

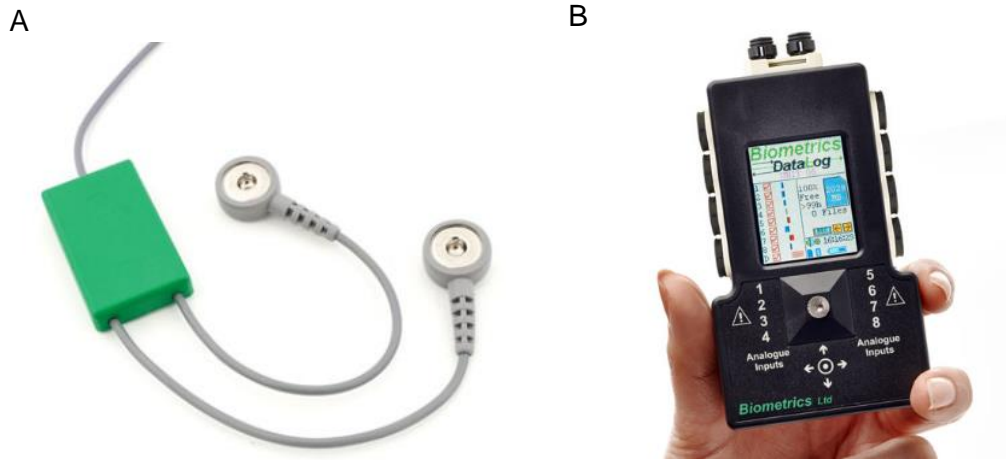


Figure 4. (A) sEMG amplifier and (B) DataLOG used in this study. (Biometrics Ltd., VA, USA. Amplifier product number SX230. DataLOG product number: MWX8.)

Triaxial Accelerometer. To record acceleration of head movements, one wired accelerometer (Biometrics Ltd., Model S3-1000G-HA) was attached to the forehead (Figure 5). The triaxial accelerometer provided simultaneous measurements in three orthogonal directions. The range of acceleration for detection is within $\pm 1000\text{G}$. Each channel of the accelerometer is automatically fitted with an 8th order 1.2 elliptic filter with a cut-off frequency of 1000Hz.

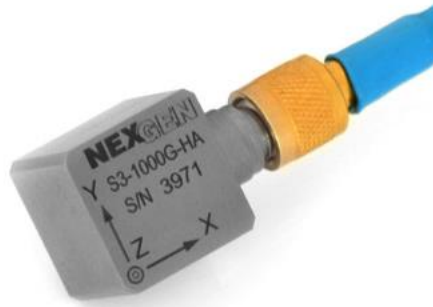


Figure 5. Wired accelerometer used for this study. (Biometrics Ltd., VA, USA, Model S3-1000G-HA, Range: $\pm 1000G$, Mass: 8g, Size: 14x13x14 mm)

Vibrator. The vibratory motors (Precision MicrodrivesTM, Model 307 – 100) used were low-voltage ($\sim 1V$) and non-invasive. For this study, vibration frequencies were between 90-110 Hz. The small electric motors were encapsulated (Figure 6). There were no moving parts that can come in contact with the skin.



Figure 6. Vibratory motor used for this study. Length: 25 mm. Diameter: 9 mm.

2.1.3 Experimental Conditions

The study involved two conditions: (1) Unrestricted dystonia, (2) VTS application.

Unrestricted dystonia: This condition recorded EMG and acceleration signals of cervical movements of participants at rest and in their symptomatic state. Vibrators were not attached to the neck, thus there was no tactile nor vibratory stimulation. Three unrestricted dystonia condition were conducted, with one at the start of the study as baseline, one after VTS condition as post VTS assessment, and one after seven minutes of retention. Comparison of sEMG and kinematic data among these three sets would indicate the efficacy of VTS on alleviating dystonic neck postures. During the unrestricted dystonia condition, participants were asked to sit and keep their head in a neutral, comfortable position. They were required not to resist the involuntary muscle

contraction and let their neck assume the dystonic posture once it was symptomatic. The duration of each unrestricted dystonia condition was 3 minutes.

VTS application: This condition aims to examine the efficacy of VTS on alleviating involuntary muscle contractions in CD. Four vibration sites were tested on the following regions: the skin above the right and left sternocleidomastoid and right and left trapezius (Figure 7). For each vibration site, two vibrators are attached and activated simultaneously. The duration of each VTS trial was initially set as 6 minutes and adjusted by the participants' response (Table 1).

Table 1. Content of VTS conditions

Sequence	Vibrator site	Duration
1	Right SCM	6 min
2	Right TRP	6 min
3	Left SCM	6 min
4	Left TRP	6 min

2.1.3 Experimental Procedure

After the completion of equipment set-up, participants performed several practice-runs to familiarize themselves with the equipment. Data collection began with an unrestricted dystonia condition as the baseline to record the initial muscle behavior during rest and symptomatic state. The VTS condition comprised four vibration sites and was applied sequentially on each vibration site (Table 1). Vibration was stopped whenever the participant reported increased pain or discomfort. The study ended with another unrestricted dystonia condition as the retention condition to record changes in cervical muscle behaviors after VTS. There was a 3-min break after each VTS condition to avoid muscle fatigue. Participants were asked to self-report the level of discomfort and the

level of effort for maintaining posture after each trial. The complete protocol is illustrated in Figure 7.

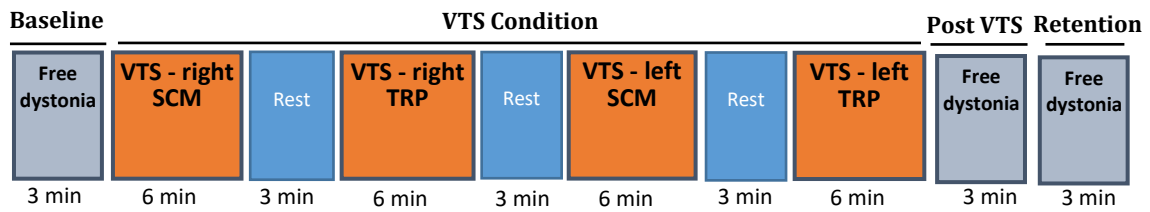


Figure 7. Complete protocol of experiment. The duration of each session is listed under the diagram. VTS: vibro-tactile stimulation. SCM: sternocleidomastoid. TRP: trapezius.

2.2 Data analysis

Surface EMG and acceleration data were collected with a sampling frequency of 1000 Hz and synchronized during data collection. MATLAB R2019a was used for data analysis.

2.2.1 Analysis of sEMG

Figure 8 demonstrates the frequency representation during dystonic episodes. Power spectral density of sEMG during dystonic episodes was higher between 3-100Hz. Raw sEMG data was filtered with a 16th order 100 Hz low-pass Butterworth filter and subsequently with an 8th order 50-70 Hz band-stop Butterworth filter to eliminate the interference caused by electrical noise.

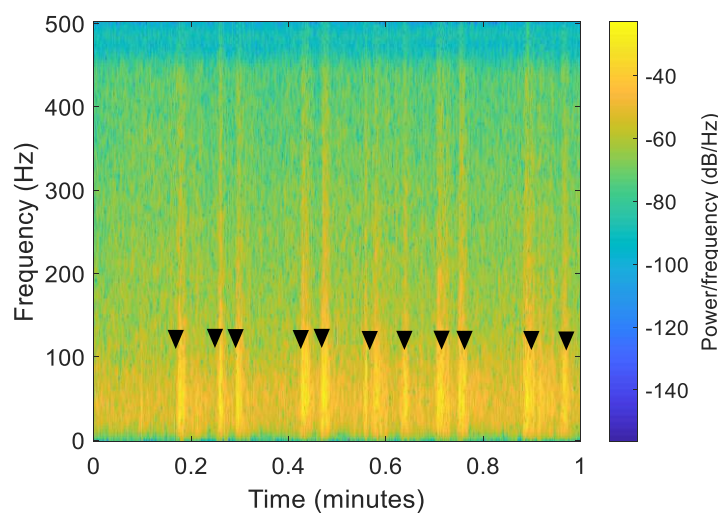


Figure 8. Surface EMG power spectrogram of right TRP in one participant. The occurrence of dystonic movements is marked with arrow on the plot. Power spectral density of sEMG is higher between 3-100Hz during dystonic movements.

Electrophysiological signatures of dystonic neck postures were identified by time-frequency analysis of filtered sEMG signal. First, time-normalized power of rectified sEMG was calculated to quantify the magnitude of involuntary neck muscle contractions. The time normalized power of sEMG is calculated as follows:

$$p = \frac{\sum_{t_1}^{t_2} x_n^2}{t_2 - t_1} \quad (1)$$

where x_n is the sEMG signal. t_1 and t_2 are time intervals.

Second, to investigate the effect of VTS on alleviating dystonic muscle activities, a percentage decrease in the power of rectified sEMG was obtained for each VTS trial by comparing to the baseline. Change in the power of sEMG is calculated as follows:

$$\text{Change in power of sEMG} = \frac{p_{ref} - p_{test}}{p_{ref}} \quad (2)$$

where p_{ref} represents power of sEMG in baseline, p_{test} represents power of sEMG in VTS condition.

Additionally, previous studies showed an increased value of CDF_{10} of EMG in dystonic muscles during isometric contraction, which reflects an increase in the energy of sEMG between 3-10Hz relative to 10-30Hz. To investigate the reliability of CDF_{10} as an indicator for dystonic muscle, CDF_{10} was obtained for all four measured muscles during unrestricted dystonia.

2.2.2 Analysis of acceleration

The kinematic of neck movements was recorded by the triaxial accelerometer in lateral, longitudinal, and vertical axis. Acceleration data was denoised down to level 6 using wavelet denoising and subsequently filtered with a 6th order 10 Hz low-pass Butterworth filter. First, to determine the peaks of acceleration that represent the dystonic neck movements, the upper envelope of the original acceleration data is obtained using spline interpolation over local maxima separated by at least 300 samples. Then the peaks of the upper envelope were filtered with a threshold of 0.3g and separated by at least 200ms, which kept peaks with amplitude above 0.3g and eliminated minor ones. The filtered peaks were then cross validated with sEMG data to ensure that they represent the actual dystonic neck movements. Second, the average number of dystonic

movements per minute (DM/min) was determined by the number of peaks in acceleration data during baseline, post VTS, and retention condition, which reflects the change in frequency of dystonic neck movements. Third, the peak amplitude of acceleration (PAA) during dystonic episodes was calculated to investigate the severity of each dystonic neck movement.

2.2.3 Statistical analysis

Statistical analysis was performed using MATLAB 2020a. CDF_{10} and PAA of dystonic neck movements are presented with median and interquartile range (IQR). A two-sample t-test was conducted to compare CDF_{10} and PAA of dystonic neck movements between conditions.

Chapter 3: Results

Given different presentations of CD on the two participants, the study protocol was modified respectively for each. To better illustrate the electrophysiological signatures and the effectiveness of VTS on these two presentations of CD, following analysis will be introduced separately for two participants.

3.1 Participant with constant retrocollis

3.1.1 Surface EMG baseline

Based on the sEMG plot (Figure 9), a constant activation was observed in left and right SCM. Given that the participant had retrocollis and SCM muscles are antagonist muscles that oppose the action of neck extension, the continuous activation in the SCM muscles provides evidence that the participant had been resisting the dystonic posture by contracting bilateral SCM. To further quantify the level of activation in SCM, the power of filtered sEMG was calculated. Power of sEMG was $0.037 \text{ mV}^2/\text{s}$ in right SCM and $0.035 \text{ mV}^2/\text{s}$ in left SCM. Additionally, although the posterior neck muscles were reported as dystonic muscles, no prominent muscle activation was observed in right and left TRP.

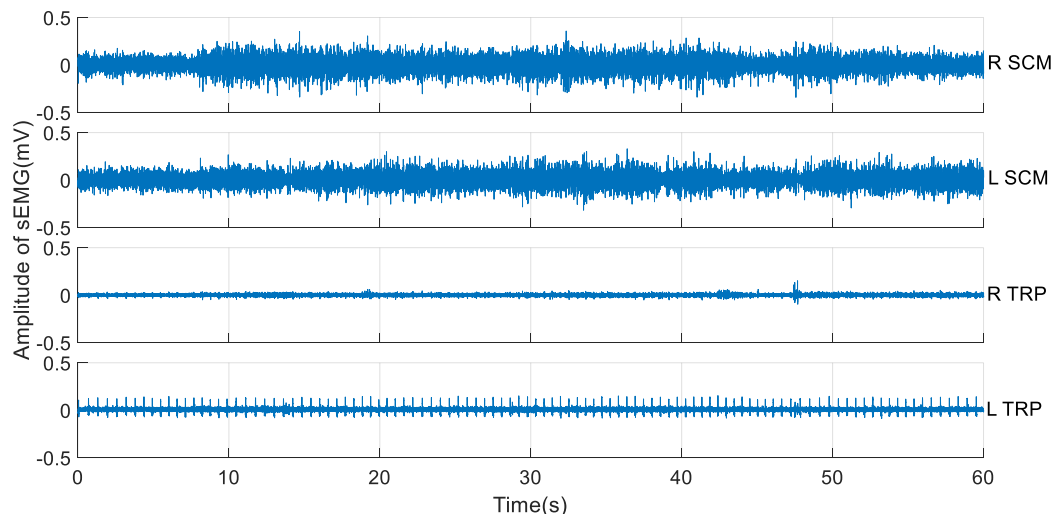


Figure 9. Raw sEMG baseline of participant with retrocollis. Constant activation was observed in bilateral SCM muscles while no prominent activation was observed in both TRP. R: right. L: left. SCM: sternocleidomastoid. TRP: trapezius.

3.1.2 Effect of VTS: sEMG and acceleration

During VTS, the participant's neck was gradually pulled backwards and maintained the dystonic posture. An example of the change in sEMG and acceleration during the process of neck extension is shown in Figure 10. The time it took from a neutral position to the extended position varies among different vibration sites from 22s to 60s (Figure 11). A consistent pattern of the increased sEMG in bilateral SCM is observed for all four vibration sites. In general, there is no clear effect of VTS on this participant with the four experimented vibration sites.

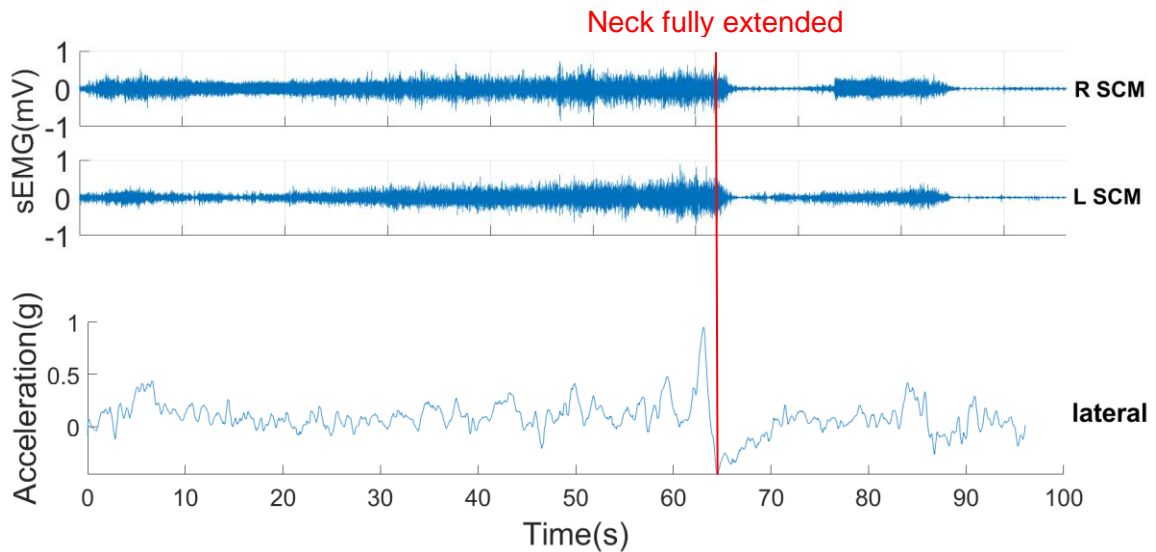


Figure 10. Change in sEMG and acceleration during VTS. Vibration was stopped at the time the neck was at full extension. Note that the amplitude of sEMG in both SCM muscles slowly increased during neck extension. A peak was observed in the lateral direction of acceleration when the neck is fully extended. R: right. L: left, SCM: sternocleidomastoid. TRP: trapezius.

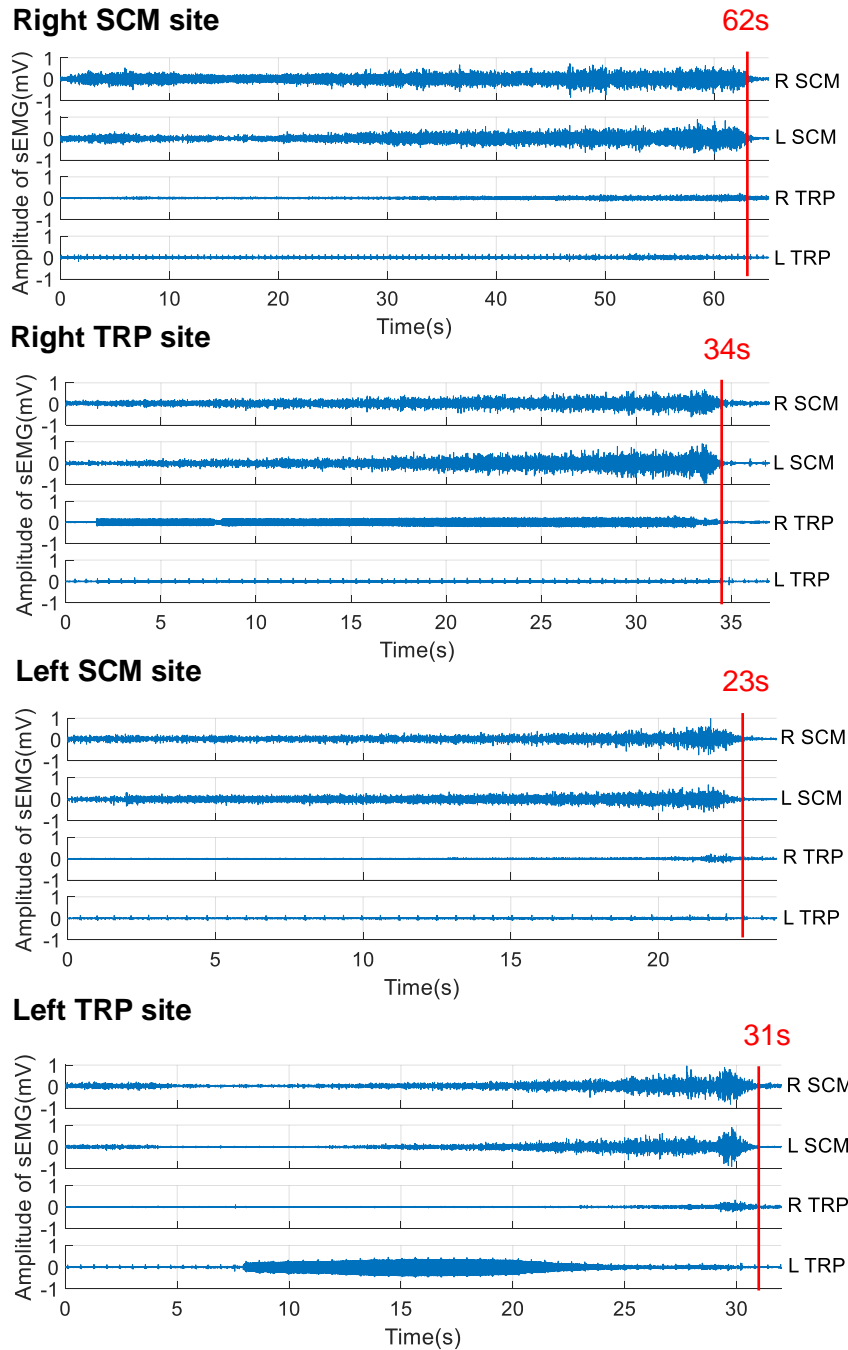


Figure 11. Effect of VTS on muscle activity for each of the vibration sites. Although the time it takes to reach the dystonic neck posture is different for each of the four vibration sites. Note that the change in sEMG follows the same pattern where the amplitude of sEMG in bilateral SCM kept increasing until the neck is fully extended. Vibration sites are listed above each plot. Muscle names are listed right to sEMG channels correspondingly. L: left. R: right. SCM: sternocleidomastoid. TRP: trapezius.

3.2 Participant with intermittent right torticollis

3.2.1 Surface EMG and acceleration baseline

Rectified sEMG with synchronized acceleration data in baseline condition is shown in Figure 12. Since participant was asked not to resist any dystonic movement and not to conduct any voluntary movements, the peaks in acceleration data reflect the occurrence of dystonic neck movements. Meanwhile, these dystonic neck movements are shown as periodic neck muscle contractions in the sEMG plot. The periodic change of sEMG is most clear in left SCM, left TRP, and right TRP, which is in line with the fact that the participant had right torticollis together with left shoulder elevation. Each involuntary muscle contraction lasted for 1-2 seconds.

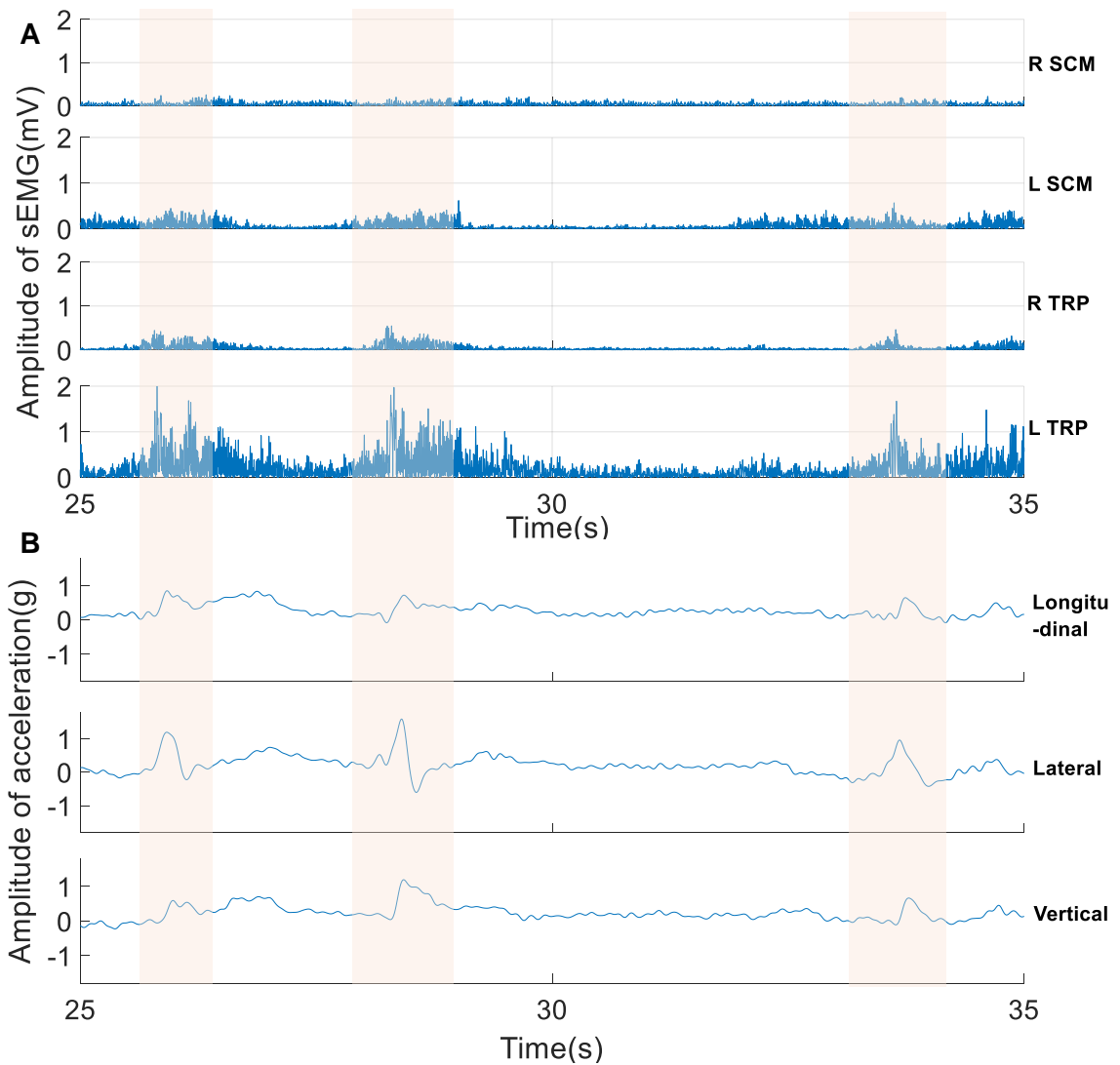


Figure 12. (A) Rectified and filtered sEMG and (B) filtered acceleration data of participant 02 in baseline condition. Data is zoomed in between 25 - 35s to better visualize the details of each dystonic movement. (A) Periodic activations are observed in Left SCM, right TRP, and left TRP. Muscle names are listed right to sEMG channels correspondingly. (B) Changes in acceleration are more prominent in lateral and vertical direction. Peaks of acceleration represent the actions of torticollis. The direction of acceleration is listed right to the plot of each acceleration channel. R: right. L: left. SCM: sternocleidomastoid. TRP: trapezius.

3.2.3 Effect of VTS: sEMG and acceleration

Surface EMG and acceleration before and after VTS

Compared to baseline condition, the frequency and average amplitude of involuntary muscle contractions decreased (Figure 13A). Meanwhile, the average peak amplitude of acceleration after VTS was observed to be lower than baseline condition (Figure 13B).

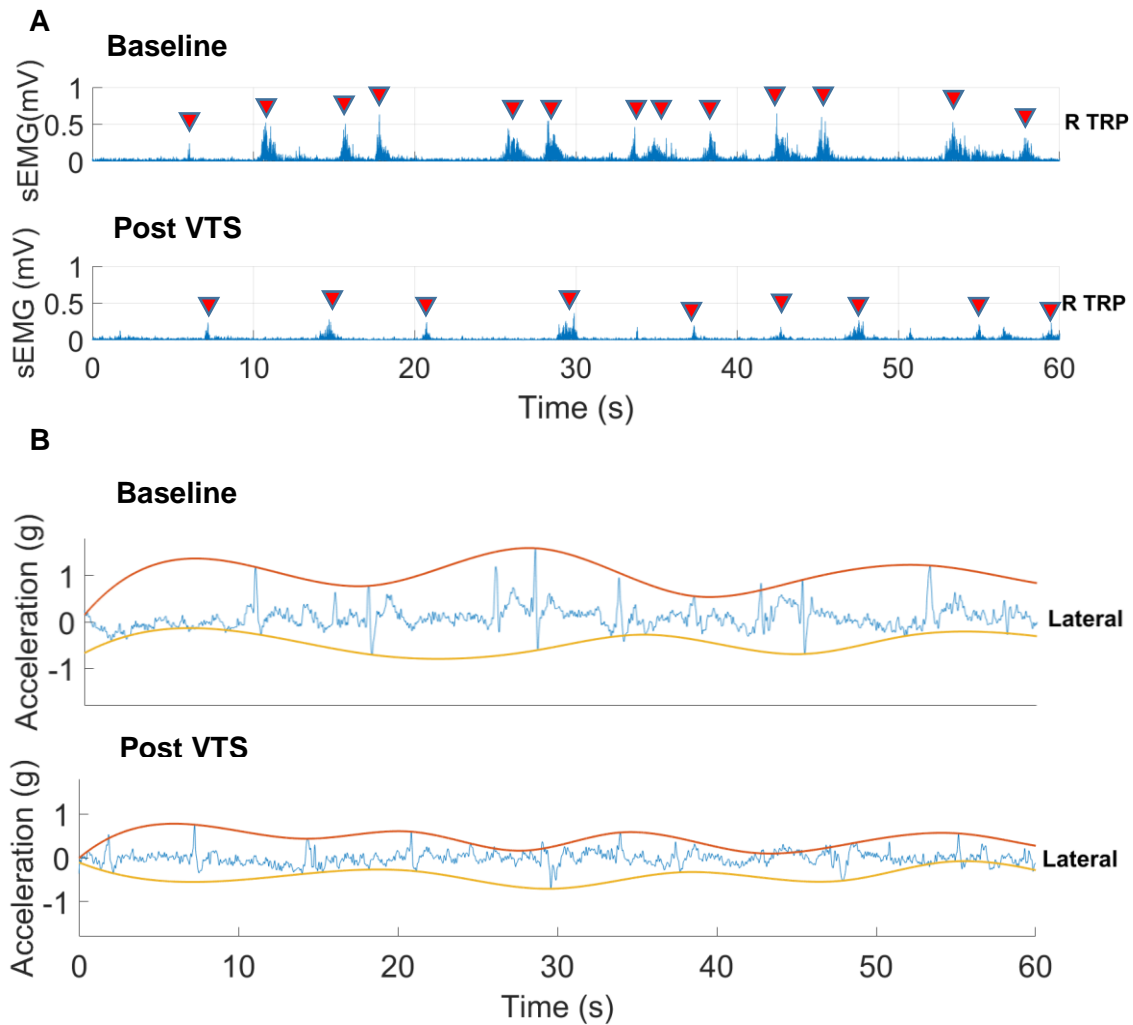


Figure 13. Changes in (A) rectified sEMG of right trapezius and (B) acceleration in lateral direction after VTS. (A) Frequency and magnitude of involuntary muscle contractions decreased. (B) Envelope amplitude of acceleration during dystonic neck movements decreased after VTS. R: right. TRP: trapezius. VTS: vibro-tactile stimulation.

Frequency of dystonic movements decreased after VTS

An average number of 15 dystonic movements per minute (15 DM/min) was recorded in the baseline condition. Compared to baseline, the frequency of dystonic neck movements decreased by 60% to 6 DM/min in post VTS condition. However, the frequency increased back to 13 DM/min after 7 minutes of retention, which is close to the frequency during baseline (15 DM/min) (Figure 14).

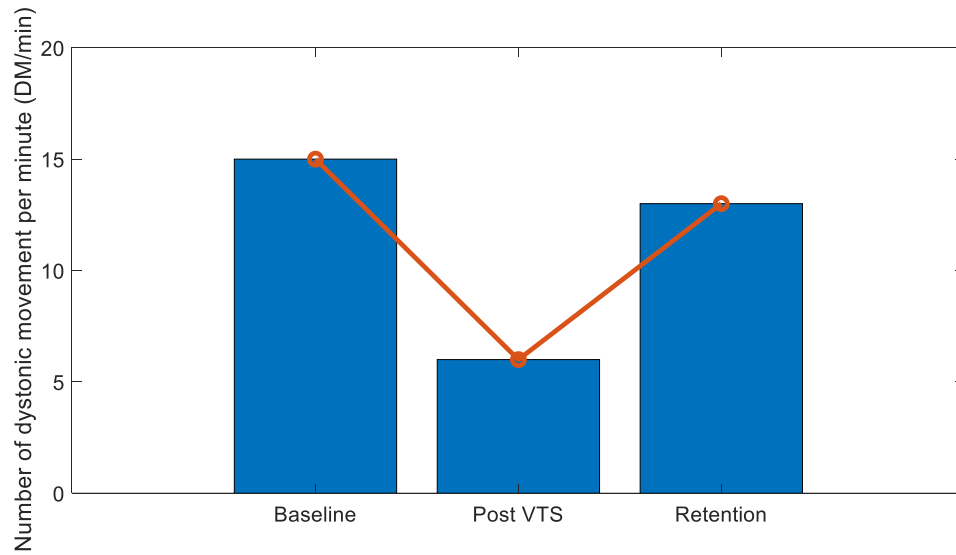


Figure 14. Frequency of dystonic movements (number of dystonic movements/min) before and after VTS. The frequency of dystonic movements decreased by 60% in post VTS condition compared to baseline and returned after seven minutes of retention.

Change in peak amplitude of acceleration after VTS

Figure 15 shows the distribution of PAA in baseline, post VTS, and retention condition. The median PAA in post VTS (median: 0.59) is significantly lower ($p < 0.01$) than the median PAA in baseline (median: 0.90). Additionally, the variability of PAA drops by 53% in post VTS condition compared to baseline. After 7 minutes of retention, the median PAA returns to the baseline level (median: 0.89).

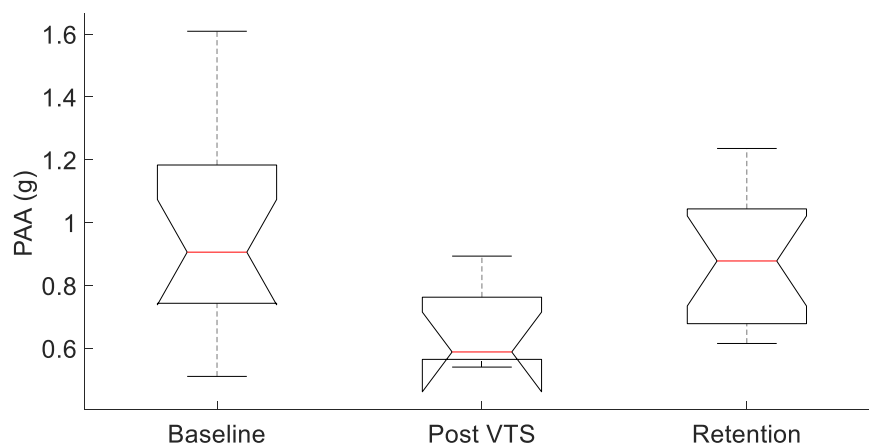


Figure 15. Peak amplitude of acceleration (PAA) during dystonic episodes in three conditions. The red line is the median, the top of the box is the 75th percentile, the bottom of the box is the 25th percentile. The whiskers represent the maximum and minimum values of peak amplitude. VTS: vibro-tactile stimulation.

Effectiveness of VTS with different vibration sites

Rectified sEMG during four different vibration sites are shown in Figure 16. **Error! Reference source not found..** For better visualization of details during dystonic movements, data is zoomed in between 0-60s.

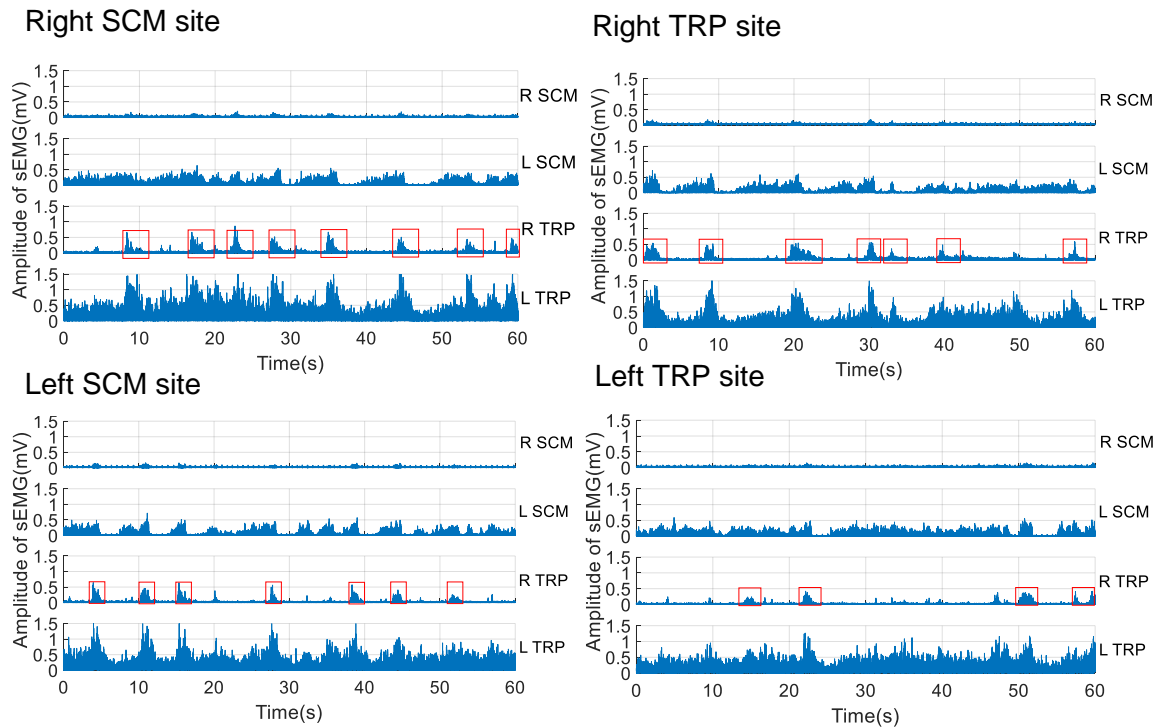


Figure 16. Decrease in the frequency of involuntary muscle contractions during four vibration sites. Each muscle activation is marked with a red rectangle. The reduction of the occurrence of dystonic muscle activities is most prominent with left TRP site. Vibration sites are listed above sEMG plots. Muscle names are listed right to sEMG channels correspondingly. R: right. L: left. SCM: sternocleidomastoid. TRP: trapezius.

To further quantify the effectiveness of VTS, change in the power of sEMG during four vibration sites is compared in Figure 17. Overall, all four vibration sites show positive rate of reduction (mean = 8.5%). Among all four vibration sites, left TRP site demonstrates the most prominent effect (mean = 14.7%) in reducing sEMG power, followed by left SCM site (mean = 10.7%). Furthermore, power of sEMG in right SCM and right TRP increased while VTS was applied on them (change in right SCM = -1.5%, change in right TRP = -5.9%). Results show that vibration on ipsilateral side of the dystonic movement (mean = 4.2%) has less reduction than vibration on contralateral

side (mean = 12.7%). Overall, left TRP shown as the optimal vibration site with the highest average change in the power of sEMG.

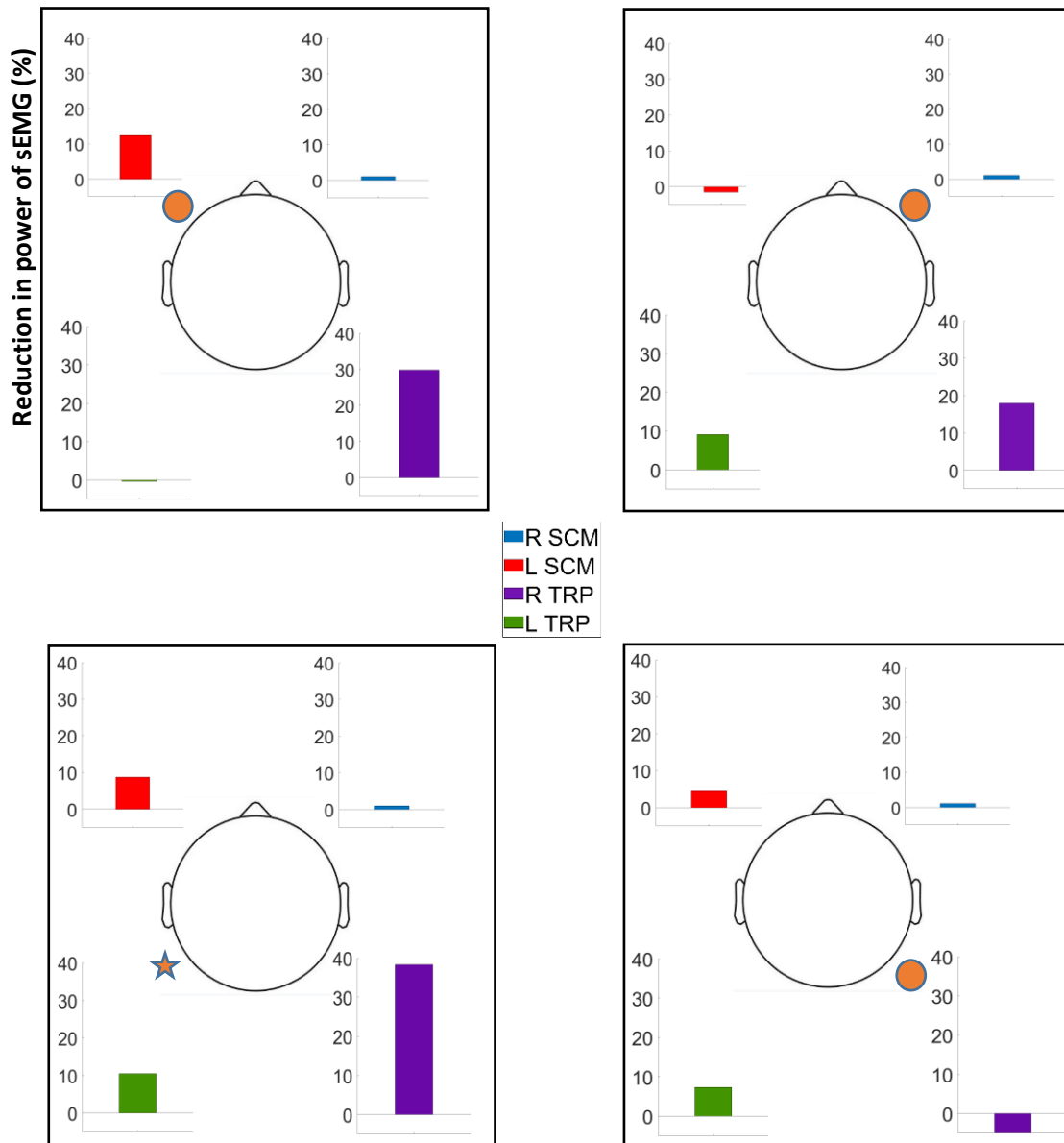


Figure 17. Change in the power of sEMG during four vibration sites. Left TRP site is shown as the optimal vibration site with the highest reduction in sEMG power (marked with star). In general, vibration on left side of neck muscles induces more change in sEMG power than right side. L: left. R: right. SCM: sternocleidomastoid. TRP: trapezius.

Though generally VTS caused reduction in sEMG power in all measured muscles, each muscle responded differently to VTS (Figure 18). Right TRP, with an average rate of

reduction of 20.1%, was observed to be the most positively responsive muscle to VTS. Left SCM and left TRP have similar rate of reduction by VTS (mean = 6.6%, mean = 6.7%). Right SCM does not seem to respond to any site of VTS (mean = 0.4%).

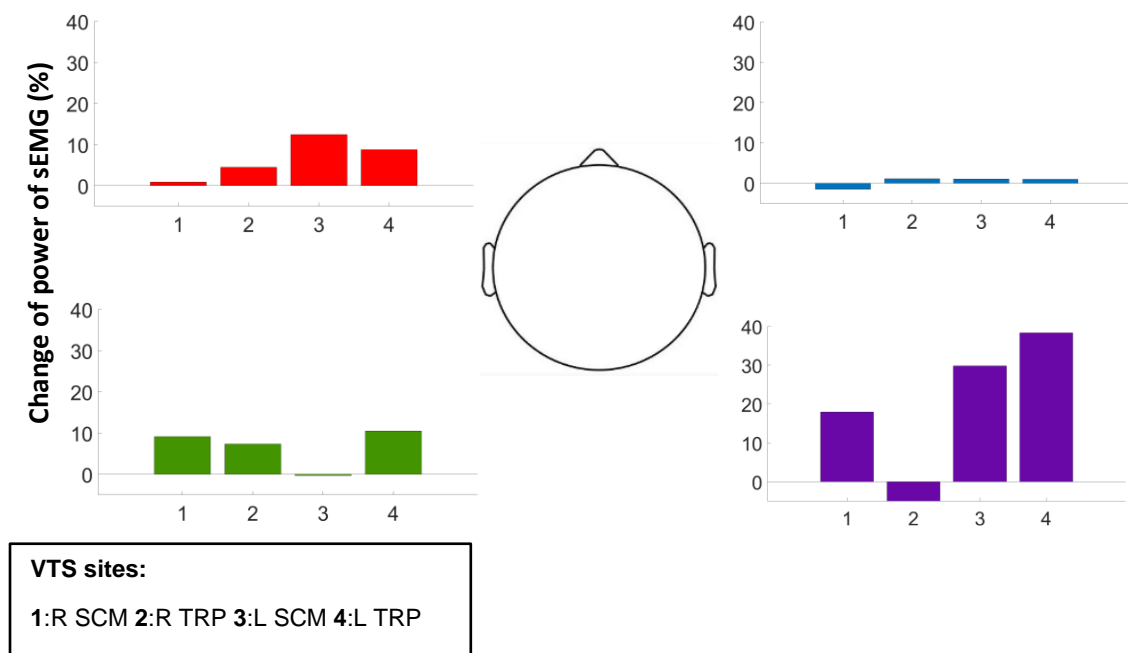


Figure 18. The response to VTS of each muscle. Change in sEMG power with different vibration sites is summarized for each muscle in the bar plot. Among four measured muscles, right TRP has the highest average reduction in the power of sEMG. Red: L SCM. Blue: R SCM. Green: L TRP. Purple: R TRP. SCM: sternocleidomastoid. TRP: trapezius. VTS: vibro-tactile stimulation.

Efficacy of VTS changed over time

Figure 19 shows how the sEMG power of four neck muscles changed over time during vibration on left TRP site. The change in sEMG power was most clear in right TRP, where a drastic decrease was observed in the first minute of vibration. A downward trend of sEMG power is found consistently in left SCM, left TRP, and right TRP, which might reflect that the efficacy of VTS was slowly accumulated over time.

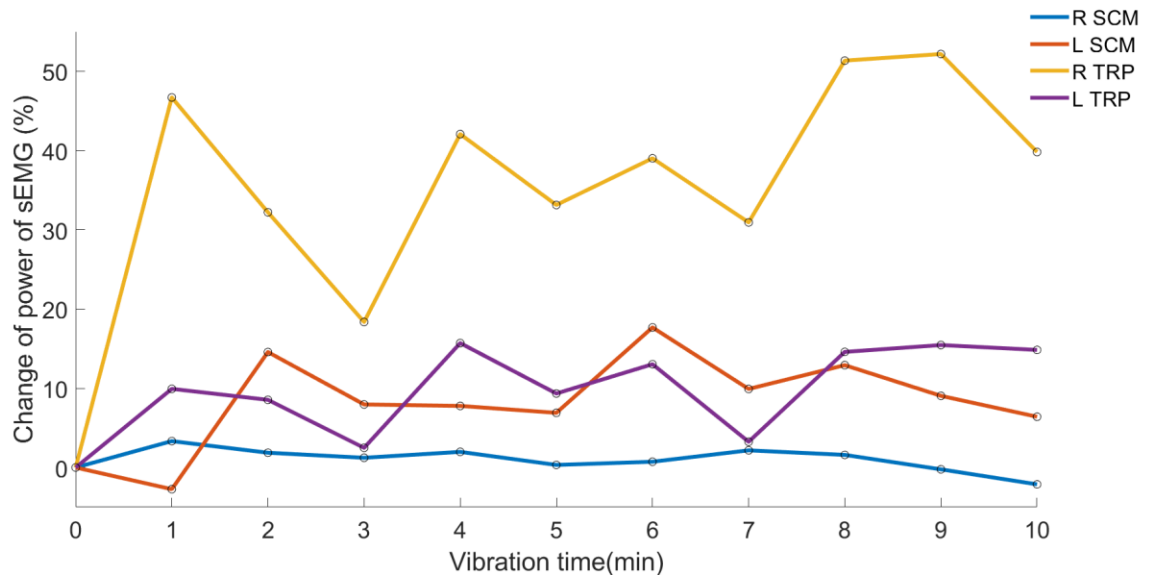


Figure 19. Efficacy of VTS changed over 10-minute vibration on left TRP site. A downward trend of sEMG power is observed in three out of four measured muscle. The change was most prominent in left TRP where the power of sEMG decreased fast within first minute. R: right. L: left. SCM: sternocleidomastoid. TRP: trapezius. VTS: vibro-tactile stimulation.

CDF₁₀ before and after VTS

Figure 20 shows the distribution of CDF₁₀ in baseline, post VTS, and retention condition. The value of CDF₁₀ of left TRP is found lower in post VTS condition (median: 0.963, IQR 0.082-0.148) than baseline (median: 0.301, IQR 0.196-0.341). The median CDF₁₀ increased after 7 minutes of retention (median: 0.117, IQR 0.101-0.213). In post VTS condition, the mean CDF₁₀ of left TRP is found significantly lower than the mean CDF₁₀ of left TRP in baseline ($p < 0.001$). Additionally, no significant difference of mean CDF₁₀ is found among four measured muscles in baseline.

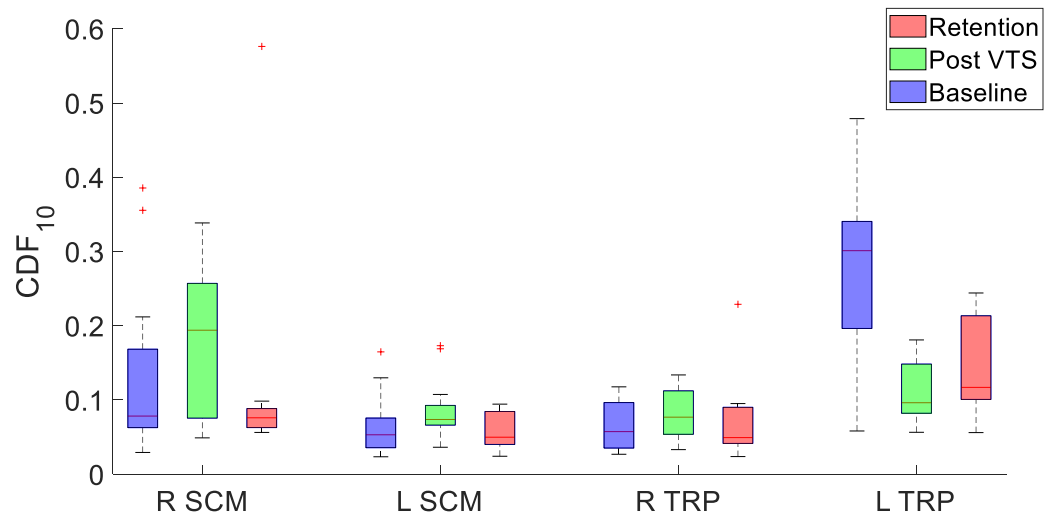


Figure 20. Distribution of CDF_{10} during baseline, post VTS, and retention condition, grouped by the measured muscle. CDF_{10} of left TRP is lower in post VTS condition than baseline. R: right. L: left. SCM: sternocleidomastoid. TRP: trapezius. VTS: vibro-tactile stimulation.

Chapter 4: Discussion

4.1 Dystonic symptoms before VTS

Two participants were observed with different presentations of CD. For the participant with constant retrocollis, the bilateral SCM were contracted constantly to resist the dystonic movement. While for the other one with intermittent right torticollis and left shoulder elevation, the dystonic neck movements were irresistible. Though involuntary activation existed in all measured neck muscles, the participant's left TRP was shown as the most affected muscle with the highest amplitude of involuntary muscle activities.

4.2 Effect of VTS on dystonic symptoms

For the participant with constant retrocollis, no improvement was observed with VTS. One hypothesis for the ineffectiveness of VTS is that the dystonic muscles are deep posterior neck muscles, which requires a higher amplitude of VTS to target. An evidence for this hypothesis is that no prominent muscle activities were recorded in TRP during dystonic episodes, which suggests that the dystonic muscle activities might exist underneath TRP.

While for the other participant with torticollis, improvements were observed in electrophysiological and kinematic features of dystonic neck movements after VTS. The clearest evidence is the decreased frequency of intermittent dystonic neck movements after VTS. Additionally, significant reduction of PAA was found after VTS, which demonstrates a decrease in the magnitude of the dystonic neck movements by VTS. As an indicator for the underlying muscle activities behind dystonic neck movements, the decrease in sEMG power of all measured muscle reflects that in general involuntary muscle contractions are alleviated by VTS. Furthermore, the efficacy of VTS was shown to be obtained in short time (<1 minute of VTS) and might slowly accumulate over time. Further investigation is needed to examine the trend of efficacy over time with a longer duration of VTS.

4.3 The role of vibration sites on the effectiveness of VTS

Four vibration sites were experimented with different effects shown on alleviating dystonic movements. Though no clear effect was observed in the participant with retrocollis, the time it took from a neutral neck position to a neck fully extended position

varied from site to site. A possible explanation for the time difference is that VTS on certain vibration sites could delay the retrocollis while vibration on other sites might trigger the retrocollis. Further studies are required to investigate the detailed influence of VTS on this participant.

For the participant with intermittent right torticollis, left TRP was shown as the optimal vibration site in alleviating dystonic movements among four sites and right TRP was the most responsive muscle during VTS condition. In general, vibration sites on the contralateral side of right torticollis (left SCM site and left TRP site) are more effective in reducing involuntary muscle activities than vibration on ipsilateral sites. One thing to notice is that during vibration on the ipsilateral side of right torticollis (right SCM site and right TRP site), an increase was found in the sEMG power of right SCM and right TRP. This deterioration in muscle spasms demonstrates that VTS on different vibration sites could induce opposite effects in the same muscle, which underlines the importance of the selection of vibration sites when applying VTS.

4.4 CDF₁₀ as a potential indicator of dystonic muscle activities

Previous studies demonstrated a shift for the power of EMG from 10-30 Hz to 3-10 Hz in dystonic muscles during submaximal isometric tasks (Bruijn et al., 2017b), where a cut-off value of 0.222 is suggested to discriminate dystonic muscle from non-dystonic muscle (Bruijn et al., 2017b). In this case study, no significant difference of CDF₁₀ is found among measured muscles. An additional finding is that the mean CDF₁₀ of left TRP in post VTS condition was significantly lower than baseline. Given that dystonic neck movements were alleviated after VTS, the significant change in CDF₁₀ suggests CDF₁₀ as a potential indicator of the underlying dystonic muscle activities.

4.5 Limitations and future studies

The outbreak of COVID-19 pandemic severely curtailed the scope of the study. A systematic investigation with larger sample size is needed in the future to validate the effectiveness of VTS for treating symptoms in CD. Another limitation is the lack of prior knowledge of VTS on CD. Although our protocol was carefully designed based on previous studies and prior experience of VTS on other forms of dystonia, part of the

study protocol was adjusted upon participants' response during the data collection to avoid causing any pain or discomfort to participants.

A confounding factor is the potential accumulative effect of VTS. As shown in the results, changes in electrophysiological and kinematic features of dystonic movements partially exist after 7 minutes of retention. Since the neck muscles were vibrated sequentially, it is possible that each VTS trial might influence the following trials. Being the last vibration site and the optimal vibration site, left TRP may have inherited effects from the previous trials. Thus, it was not systematically clear if the change in sEMG power was the result of a single VTS trial or the whole VTS condition. Future studies with randomized sequence of VTS would reduce this bias.

In this case study, only one configuration of vibration amplitude was applied. As was discussed for the participant with retrocollis, low amplitude of VTS might not be able to target deeper neck muscles such as splenius capitis, which might have limited the effect of VTS. Further studies need to experiment different vibration amplitude to target deeper cervical muscles.

Chapter 5: Conclusion

This proof-of-concept study examined the effect of VTS on alleviating the involuntary cervical muscle contractions in two participants with different presentations of CD. The application of neck muscle VTS did not induce meaningful symptom relief for the participant with constant retrocollis. While for the participant with right torticollis, the frequency and extent of the dystonic postures were markedly reduced during and immediately after VTS application. Furthermore, the effectiveness of VTS in alleviating dystonic muscle spasms depended on vibration site. Future studies are required to systematically investigate the effectiveness of VTS on CD with larger sample size.

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