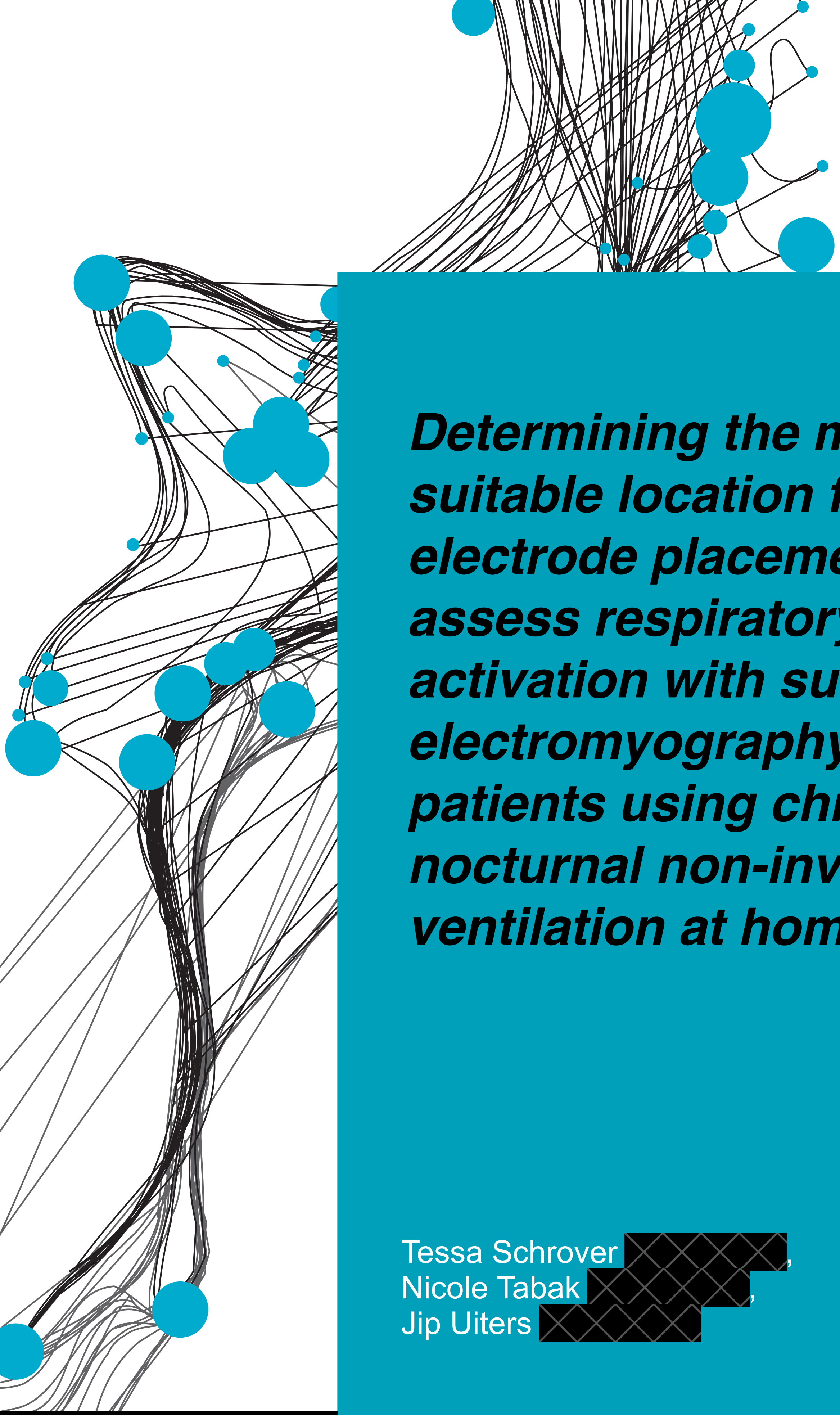

Determining the most suitable location for electrode placement to assess respiratory muscle activation with surface electromyography in COPD patients using chronic nocturnal non-invasive ventilation at home.

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ABSTRACT

0.1 Rationale

This study aims to assess the suitability of different electrode locations using sEMG of respiratory muscles for monitoring patients with COPD using chronic nocturnal non-invasive ventilation at home. The main research question is to identify the most optimal sEMG electrode location to measure muscle activation during respiration.

0.2 Methods

The research started with a comprehensive literature review. After the initial literary review, two experiments were conducted. These experiments involved measuring sEMG activity in previously identified locations on the respiratory muscles of individuals. The first experiment that was conducted was done on two healthy individuals so the researchers could become acquainted with the equipment, and it aimed to narrow down the variables involved. The second experiment focused on an individual with COPD on NIV and aimed to draw more specific conclusions for the research. The collected data was analyzed using a high-pass filter and RMS modification. Conclusions were drawn based on the reviewed data.

0.3 Results

After an initial review of the literature, certain respiratory muscles were found unsuitable for the study. This decision was based on practical considerations and the lack of evidence supporting their suitability as described in literature. From this search, it was determined that the following muscles would undergo further testing: two locations on the parasternal intercostals, two locations on the diaphragm, one location on the scalene, and two locations on the sternocleidomastoid. As a result of the first experiment, certain locations were excluded from the second experiment, as they proved to not give a reliable signal. Only three locations remained for testing in the second experiment: one placement on the diaphragm, one placement on the parasternal intercostal muscles, and one placement on the sternocleidomastoid. The second experiment gave positive results for all muscles tested, particularly the diaphragm leads placed bilaterally on the anterior axillary line.

0.4 Conclusion

This study provides valuable insights into the suitability of different respiratory muscles for sEMG monitoring of COPD patients. The diaphragm and parasternal intercostals with established electrode placement protocols can provide reliable sEMG signal for respiratory activation monitoring. Further research is needed to explore the practical implementation and validate these findings in clinical settings.

CONTENTS

1 INTRODUCTION

If you are breathing, you are using your respiratory muscles to make that happen. The primary muscles are the most important and work in every healthy individual. The accessory muscles are only active when the primary muscles need help, this can happen during exercise or with lung or neuromuscular diseases for example. During inhalation, the most important primary respiratory muscle, the diaphragm becomes active. When it contracts it enlarges the intrathoracic volume and widens the thorax [1]. Consequently, the intrathoracic pressure decreases, enabling the expansion of the lungs and the intake of air [1]. During exhalation, the diaphragm remains passive unless there is resistance present. This is due to the elastic recoil of the lungs and the decompression of the abdominal viscera [2]. The other primary respiratory muscles are the internal and external intercostal muscles. The intercostal muscles consist of different layers: the superficial layer and the internal layer [2]. The external intercostal muscles are located in the superficial layer. These muscles run infero-anteriorly from one rib to the rib directly below it. Due to their direction, they are primarily active during inhalation [2]. The internal intercostal muscles are located in the internal layer and run perpendicular to the external intercostal muscles. Due to the direction in which the muscles run, they are primarily active during exhalation [2].

The accessory respiratory muscles can be divided into several groups. The axio-appendicular muscles, extending from the chest to the upper limbs, serve as accessory respiratory muscles by elevating the ribs during deep inhalation [2]. Another group includes the oblique neck muscles, such as the scalene and sternocleidomastoid muscles, which assist in elevating the ribs during forced inhalation and contribute to neck movement [2]. The remaining intercostal muscles, known as the muscles of the thoracic wall, support the intercostal spaces and thoracic cavity. These muscles, including the serratus posterior, levator costarum, subcostalis, and transversus thoracis, are active during both inhalation and exhalation, with a primary role in forced breathing [2].

Patients with Chronic Obstructive Pulmonary Disease (COPD) experience significant difficulty in breathing. COPD is a progressive lung condition characterized by chronic bronchitis and emphysema, often resulting from smoking or exposure to harmful substances. It leads to increased airway resistance and loss of elastic recoil of the lungs [3]. The severity of COPD is determined through spirometry tests, and advanced stages may lead to chronic respiratory failure [4]. The burden on the lungs triggers the activation of accessory respiratory muscles, while the weakening of the diaphragm contributes to respiratory limitations [5]. Pathological changes in the diaphragm affect its mobility, strength, and coordination, further deteriorating respiratory function in COPD [6-8].

Patients with COPD have limited treatment options. Non-invasive ventilation (NIV) can benefit these patients by allowing their respiratory muscles to rest and reducing PaCO2 levels, resulting in improved quality of life during the day. One of the primary applications of nocturnal home NIV (NH-NIV) is the treatment for chronic hypercapnic respiratory failure (CHRF) in patients with COPD or neuromuscular diseases [9]. Especially patients who are in an advanced stage of COPD experience CHRF [9]. Patients with CHRF have chronically elevated PaCO2 levels, primarily due to alveolar hypoventilation caused by increased airway resistance and pulmonary hyperinflation [9]. The elevated PaCO2 level leads to respiratory acidosis in the body. High-intensity NIV improves blood gas values and reduces the burden on patients during the night by taking over a significant portion of the ventilation. What sets ventilation for this patient group apart from ventilated patients on the intensive care unit is that the main goal is not to wean patients off nocturnal ventilation but to provide complete support [10]. However, during the daytime, PaCO2 levels will rise again, increasing the burden on the lungs, which will then be reduced through ventilation during the night once again [10]. Therefore, it is crucial to adjust the ventilation device to each specific patient's physiology. Typically, the settings of the ventilation device are determined during a hospital visit and reviewed every six months at the home of the patients. However, between these reviews, patients cannot be effectively monitored due to the lack of an ideal set-up [11].

Currently, the evaluation of NIV relies on parameters such as flow, pressure, and saturation. However, there still is a need for more extensive monitoring. To enhance home monitoring, additional parameters such as EEG, oxygen saturation, and EMG may be considered in the future. However, there is still a lot of uncertainty which parameters can effectively monitor the patients' conditions [11, 12]. An ideal scenario would involve a feedback system within the machine itself to make necessary adjustments, although right now this is only a hope for the future. Surface electromyography (sEMG) appears to be a relatively simple and noninvasive method to measure ventilation in a comfortable way for patients. Electromyography (EMG) is a technique used to measure the electrical activity of muscles. It can be applied to respiratory muscles through intramuscular (imEMG), transesophageal (teEMG), and transcutaneous (sEMG) methods [13]. While imEMG provides minimal noise but is invasive, teEMG is uncomfortable and primarily used in intubated patients. sEMG is non-invasive but susceptible to noise between the skin and electrode.

The challenges in using sEMG for measuring respiratory muscles can mostly be found in the significant interference from the electrocardiography signal (ECG), which has much larger amplitude than the activity of the respiratory muscles [13]. Processing sEMG signals is complex not only due to cardiac interference but also due to noise and motion artifacts. Nonetheless, filtering techniques have been developed to separate the muscle activity of the respiratory muscles from the acquired signal [13]. Besides this, while sEMG is already used clinically for diagnostic research on neuromuscular disorders of skeletal muscles, its application for respiratory monitoring is still in the early stages. Since 1999, guidelines for electrode placement on 27 skeletal muscles have been established by SENIAM (Surface EMG for Non-Invasive Assessment of Muscle) [14]. However, electrode placement for respiratory muscles is not yet standardized, and different locations are used in clinical trials, limiting generalizability of results [15]. By establishing guidelines for electrode placement and providing transparency in filtering methods, the clinical application of respiratory sEMG can be accelerated. The aim of this study therefore is to make an assessment about the most optimal placements of the sEMG electrodes for monitoring the activity of the respiratory muscles.

The following research question is formed: *What is the most suitable location of sEMG electrodes on the respiratory muscles in patients with COPD using chronic nocturnal non-invasive ventilation at home, in order to measure muscle activation for respiration?*

For answering this question several subquestions were formed:
- *Out of which respiratory muscle(s) can the most information about respiration be obtained using sEMG during chronic nocturnal ventilation in patients with COPD?*
- *Which factors should be considered when setting up sEMG measurements for the selected respiratory muscle(s) during chronic nocturnal ventilation in patients with COPD?*
- *How is muscle activation during chronic nocturnal ventilation reflected in the sEMG signal after filtering?*

2 METHODS

2.1 Assessing the respiratory muscles for use with sEMG

The first step in the research was to assess the suitability of the primary and accessory respiratory muscles for sEMG measurements. For answering the first subquestion a literature review was performed. The search started broad with a list of all respiratory muscles and those were researched further in order to either in- or exclude them.

The literature review was conducted using PubMed database, Scopus and Google Scholar during the period of May 2023. The search terms that were included can be found in the appendix (see Appendix A.2.1). Not every article from the search results was used. The team assessed if the article was relevant. Every study that was included contained some information about either the use of sEMG on a respiratory muscle or about the activation of the muscles for breathing with COPD, or a combination of both. With the information from the articles the team drew conclusions which muscles they would investigate further, and which muscles can be eliminated.

2.2 Determining the electrode placement per muscle

After the first line of research, the goal of the second phase was to determine the various locations of the sEMG electrodes on the suitable primary and accessory muscles. This was accomplished through a literature review that was more focused and specified than the first phase. The search aimed at identifying specific protocols for different locations of the electrodes used in other studies.

The literature review was conducted using PubMed database, Scopus and Google Scholar during the period of May 2023. The search terms that were included can be found in the appendix (see Appendix A.2.2). Not every article from the search results was used. Only studies that specifically used sEMG for respiratory muscles were used. Based on the information gathered from the articles, the team developed an experimental protocol incorporating the locations found.

After completing the literature review to expand the range of knowledge, the team conducted a series of experiments. The initial set of experiments began with a low-key approach, involving the researchers themselves. This approach served two purposes: first, to become acquainted with the EMG apparatus, and second, to address specific knowledge gaps that were not covered in literature. The second set of experiments involved a COPD patient at the Universitair Medisch Centrum Groningen (UMCG), primarily aimed at validating the findings obtained from the first experiment with the experiments on the COPD patient.

With both experiments the preparation of the skin, before applying the electrode, was done by scrubbing with an alcohol wipe. Research has shown that adding gel has no additional value and even introduces additional motion artifacts [16, 17]. However, it has been found that skin preparation with alcohol scrubbing does make a significant difference in the signal [16].

In literature there was some evidence that the position of the patient could have an influence on the sEMG signal. This is particularly important for the sternocleidomastoid muscle because it is also involved in head movement and stability. These studies have shown that there is clearer muscle activity when the patient is in a lateral decubitus position compared to standing, seated, and supine positions [18, 19]. In this study only the supine and lateral decubitus positions will be considered as a variable since the patient is sleeping.

2.2.1 Experiment 1

Subjects

Two healthy students that were part of the research team were included. All participants were informed about the purpose of the study and gave verbal informed consent. The study was approved by the University of Twente Natural Sciences and Engineering Sciences Ethics Committee.

Experiments

Seven sEMG measurements were performed on each participant using the TMSi porti system. The activity during breathing is measured in the parasternal intercostals (2x), diaphragm (2x), scalene (1x) and sternocleidomastoid (2x) by using the set-up described in the experimental protocol (see Appendix A.3). The participants were asked to lay completely still during the measurements to try and avoid movement artifacts. During the measurements, the participants breathed through one straw. This way an attempt was made to simulate the restricted airways of patients with COPD [20]. Based on the literature review, the different variables that were considered are position and the location of the ground electrode: lying in supine or lateral decubitus position, and the ground electrode placed on either the sternum, clavicula or the wrist.

Data analysis

All measurements are filtered with a bandpass filter of 200Hz-400Hz and plotted. The respiratory rate was 15 breaths per minute, using a metronome. This way, the breaths can be detected from the plotted sEMG signal since there is one breath every 4 seconds. For evaluating the signals, multiple breaths were analyzed. The lesser parts of the sEMG signal were also analyzed to draw a non-biased conclusion.

2.2.2 Experiment 2

Subjects

One patient in the pulmonology department of the UMCG with COPD was included in the experiment. The participant was informed about the purpose of the study and gave verbal informed consent. The study was approved by the UMCG.

Experiments

One sEMG measurement was performed on the patient using the Dipha system. In this measurement there were 6 leads, used to measure 3 different muscles. The activity of the respiratory muscles is measured in the parasternal intercostals, diaphragm and the sternocleidomastoid by using the set-up described in the experimental protocol (see Appendix A.4). The patient was in the hospital in order to start with NIV so he could get the right settings and practice with the mask. During the measurement the patient was asked to follow instructions regarding position and breathing.

Data analysis

The Dipha system automatically produces a root mean square (RMS) signal of the leads, next to the raw data which has a 20 Hz high-pass filter. To analyze the data, the produced RMS signals were plotted in the same graph as the airway pressure to examine whether the peaks correspond with each other. Furthermore, the area under the curve (AUC) was calculated to quantify the signals.

2.3 Signal interpretation

After the experiments were completed, the team evaluated the results. To analyze the data, an understanding of all components in the signal was necessary to find an effective filtering technique. The researchers used their existing knowledge and combined this with a literature review. This review aimed to identify an effective filtering method to easily filter the signals obtained from the experiments.

The literature review was conducted using PubMed database, Scopus and Google Scholar during the period of June 2023. The search terms that were included can be found in the appendix (see Appendix A.2.3). Only studies that specifically said something about the use of a high-pass filter to filter out the ECG signal, preferably measuring sEMG of the respiratory muscles, and studies about noise-factors in sEMG were used. Based on these results, the team chose the best way to filter the signals from the experiments.

3 RESULTS

3.1 Assessing the respiratory muscles for use with sEMG

During the examination of various accessory respiratory muscles for compatibility with this study, certain muscles were found to be unsuitable due to practical reasons. The m. serratus posterior and m. levator costarum, cannot be effectively monitored using sEMG, because the electrodes need to be placed on the patient's back [2]. This is because the back region is uncomfortable for patients during the night and can cause artifacts in the monitoring system, which is not ideal for a study focused on nocturnal ventilation. Because of the location, the m. transversus thoracis and m. subcostalis, located beneath the ribs, also aren't suitable for measuring muscle activity with sEMG [2]. These muscles are also among the least used for breathing. Therefore, including them in the study is not suitable [2].

Other muscles can also be excluded from this research based on previous findings indicating their unsuitability for monitoring with sEMG. One of them, the inferior part of the m. serratus anterior, has been found to be active as an accessory respiratory muscle [21]. Although this muscle is investigated related to exercise, it is not commonly studied in sEMG research related to respiratory movements [21]. Other studies have explored the potential of measuring the m. pectoralis major for respiratory activity. While it can contribute to respiratory movements in cases of respiratory failure, its primary role is to stabilize the ribcage [22, 23]. As a result, its suitability for this study remains uncertain, but the team chose to exclude it because there are other more promising muscles to use in this study.

Four of the respiratory muscles remain suitable for further research in this study. One of them is the sternocleidomastoid muscle. The efficacy of using the sternocleidomastoid for measuring respiratory activity depends on factors such as the patient's position and breathing type [18, 19, 22]. In healthy patients, the sternocleidomastoid is typically inactive at rest, and several studies concluded that in most patients with COPD, the sternocleidomastoid remains inactive [24-26]. It is important to note, however, that when considering a COPD patient for NIV, their COPD is in a severe state, indicating that the SCM could be actively engaged in most cases.

Another suitable muscle is the anterior scalene muscle. Previous studies of the scalene muscle concluded that it gives a reliable signal of EMG activity [27, 28]. Chiti et al. (2008) researched sEMG electrodes on one side of the patient and imEMG electrodes on the other side, and concluded that sEMG and imEMG had a high degree of similarity [27]. imEMG was considered to be the golden standard in this study [27].

In literature the parasternal intercostal muscles, mostly active during inspiration, have also been found to measure the neural respiratory drive (NRD), an approximation of muscle activation [29-33]. Different locations of electrode placement have been used in previous studies, with the second intercostal space being the most common placement for sEMG electrodes [31, 34-41]. The second intercostal space was specifically chosen because the fractional shortening of the parasternal intercostal muscles decreases gradually from the second to the fifth interspace [42]. Therefore, the second intercostal space is considered to give the best signal.

Different types of study designs were found that assessed the suitability of the use of sEMG for the diaphragm for monitoring respiratory activation in comparison with established standards. Multiple studies have shown a strong correlation between sEMG and teEMG, particularly in high NRD cases like COPD patients [41]. Additionally, articles conclude that electric activity of the diaphragm can be reliably monitored by sEMG on intubated patients undergoing assisted mechanical ventilation. This provides data that is comparable with the transesophageal technique [30, 43]. Furthermore, Sarlabous et al. (2019) found a strong correlation between the neural onset of the sEMG and exerted pressure [44].

In conclusion, this review suggests that sEMG of the sternocleidomastoid, scalene, parasternal intercostals, and diaphragm can be a reliable tool for monitoring respiratory onset in COPD patients, potentially enabling telemonitoring and identification of ventilation issues.

3.2 Determining the electrode placement per muscle

3.2.1 Literature review

After looking at the different muscles, the next step was to look at the different locations of the exact electrode placements. For each muscle, various protocols regarding the exact electrode placement were found.

For the diaphragm, one of the protocols used the lower (inferior) costal margin, bilaterally on the midclavicular line [43, 45, 46]. Another protocol located the electrode placement at the right anterior axillary line and left anterior axillary line [41].

When measuring the parasternal intercostals, most of the studies used an almost identical positioning of the electrodes. Some studies used a placement bilaterally 3 centimeters away from the sternum in the second intercostal space [47, 48]. But others counted the 3 centimeters from the middle point of the sternum or 2 centimeters from the side [31, 49].

For the scalene muscle, the studies that were found used the same placement protocols. The electrodes were placed on the posterior triangle of the neck on the right, where an inter-electrode distance of 1 centimeter was maintained. The cricoid cartilage was used as a reference point for positioning the electrodes specifically for the anterior scaleni muscle [27, 28, 50].

Several protocols for placing electrodes on the sternocleidomastoid were found. In the first study, the electrodes were placed at the intersection of the upper one-third and the lower one-third of the muscle with a distance of 3-5 cm in between [22, 41]. In another study the electrodes were placed as a linear array of four electrodes starting from the right sternal head of the sternocleidomastoid and the anterior scalene [51-53].

The electrode locations were all determined based on anatomical landmarks and muscle palpation to ensure accurate placement. In most of the studies, proper preparation of the skin was done before electrode placement, although this was not discussed in every study. The skin was shaved and scrubbed, sometimes the skin was also cleaned with alcohol to reduce impedance, and conductive gel was applied to improve electrode-skin contact.

Apart from variances in electrode placement for each specific muscle, there are also differences in the location of the ground electrode. There is limited literature about the effect of different placements of the ground electrode. From a physiological standpoint, the specific location of the ground electrode may not significantly impact the results. However, in practical terms, its placement could potentially influence factors such as proximity to the heart. In the literature, the most mentioned locations for the ground electrode are at the wrist, clavicula, and the manubrium sterni [45, 54, 55]. In one instance, the ground electrode for measuring the sternocleidomastoid was positioned on the ankle [51].

Based on these findings, seven locations were chosen to be included in the first experimental protocol. These included specific locations of two parasternal intercostal placements, two diaphragm placements, one scalene placement and two sternocleidomastoid placements (see Appendix A.3). Three different ground electrode locations were used, on the wrist, the clavicula and the sternum. The results are discussed in the section below.

3.2.2 Experiment 1

Ground electrodes

For observing the results of three different ground electrode placements, the obtained signals were plotted alongside each other per muscle. It is important to note that the analysis is based on visual observations rather than numerical data. This is because different measurements, not conducted during the same time period, were analyzed and minor variations due to slight changes in position and breathing can result in subtle differences in the signals. Most signals show almost no variation between the different ground electrodes. In some measurements, it appears that the placement of the ground electrode on the sternum provides a higher amplitude than the others, but the difference is not significant enough to conclude that the remaining ground electrodes provide poor signals. Another thing that should be considered is that in the measurements of experiment 1, the subject was asked to lie completely still, however, when a patient is sleeping, they will not be completely still throughout the night. This could mean that the electrode on the wrist can cause more movement artifacts. We conclude that in this serie of measurements, the ground electrode location does not make much of a difference in the reliability of the signal. For further research and measurements in the UMCG, the ground electrode will be placed on the manubrium sterni.

Position

The change between the supine and lateral decubitus position caused different results per muscle. It is important to note that in this analysis there might also be slight variations because the measurements were not conducted during the same time period. Both the parasternal intercostals leads exhibited the most preferable signals when the subject was in supine position (see Appendix A.5, figure A.3). These signals were deemed preferable because the amplitude of the inspiratory phase is higher than when the subject is in lateral decubitus position, where the amplitude of the expiratory phase is just as high as the amplitude of the inspiratory phase. However, the respiratory rate (RR) is still distinguishable in both positions. The diaphragm leads showed the most preferable signals when the subject was in lateral decubitus position (see Appendix A.5, figure A.4). The inspiratory phase has higher amplitudes and a lower amount of chatter than in supine position. The measurements from both positions showed a distinguishable RR. For the first location on the sternocleidomastoid, the best position turned out to be the lateral decubitus position. This is because in this position the RR is distinguishable, while there is no RR visible on the measurements when the subject is in lateral decubitus position. For the second location of the sternocleidomastoid, this is the other way around (see Appendix A.5, figure A.5). The best position for this muscle is the supine position, because this way there is a distinguishable RR, while there is no RR visible in lateral decubitus position. Unfortunately, the scalene gave poor signals in both positions, where no RR could be detected (see Appendix A.5, figure A.6).

Comparison of electrode locations

Out of the two different electrode placements of the parasternal intercostals, it was found that there isn't much of a difference between the obtained signals (figure 3.1). The expiratory phase of the P2 location had a slightly higher amplitude than seen in the P1 location, this could be explained by crosstalk from the internal intercostals, active during expiration. The conclusion therefore is that placing the electrodes 3 centimeters from the midpoint of the sternum or the sides of the sternum doesn't make too much of a difference.

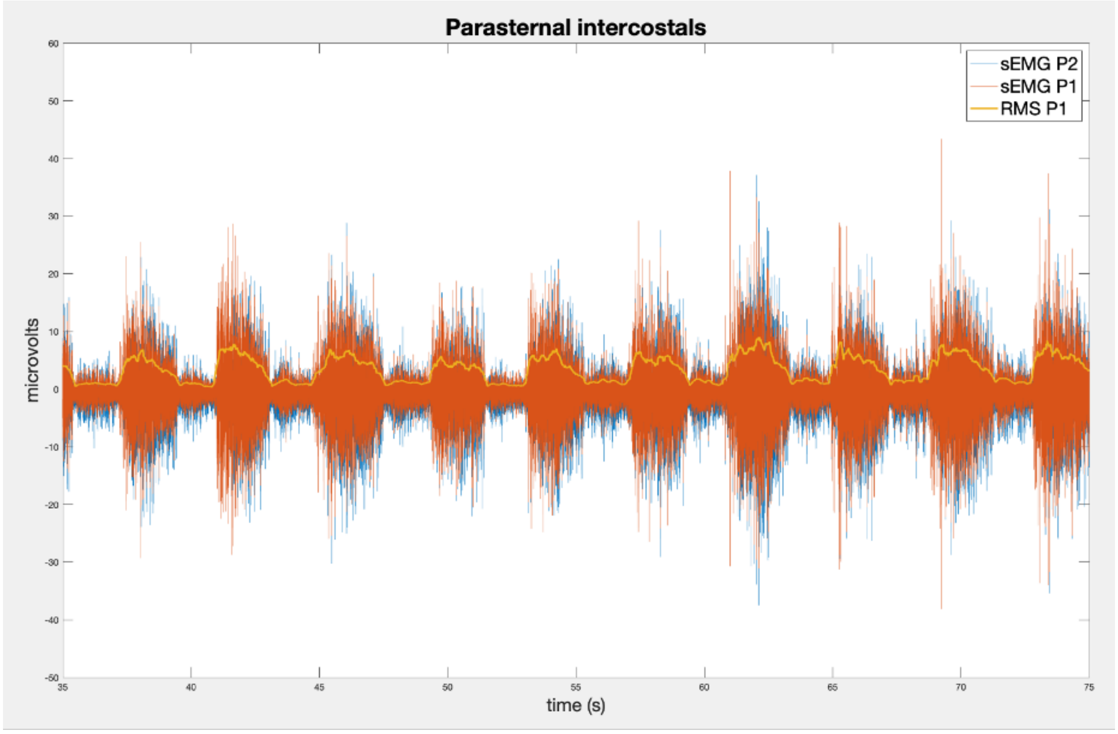

Figure 3.1: *Signal of two different EMG electrode placements on the parasternal intercostal muscles.*

For measuring the activity of the diaphragm, two different electrode placements were examined, and it was found that the signals overlapped for most parts, but the D2 location measured a greater amplitude difference between the inspiratory and expiratory phase which makes it easier to detect the NRD (figure 3.2).

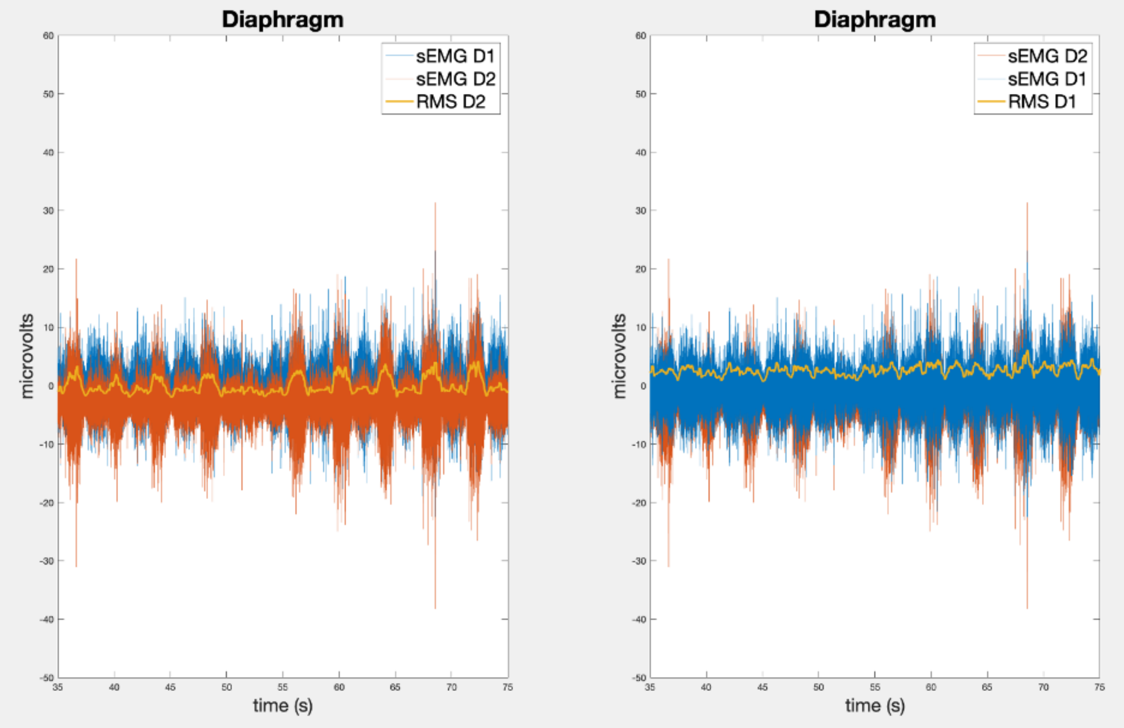

Figure 3.2: *Signal of two different EMG electrode placements on the diaphragm.*

The scalene measurements were found to be unreliable. The amplitude was 10 times higher than the amplitude of all the other muscle measurements and no distinct respiratory drive was detected. The sternocleidomastoid, however, showed a clear expiratory and inspiratory phase. The SCM2 location measurements were found to be more reliable during measurements in supine position, while the SCM1 location measurements were found to be more reliable during measurements in lateral decubitus position.

Conclusively, the D2 seems to give the most reliable signal, with the highest inspiratory amplitudes in both positions. The parasternal intercostals are even better when the subject is in supine position, but not as good as the D2 when the subject is in lateral decubitus position. The sternocleidomastoid is dependent on the body position, but either way the signal from D2 was received as a better signal. Lastly, the scalene did not show any signs of a pattern that could correspond with the respiratory rate. For further measurements on a COPD patient, the second location of the diaphragm (D2), the second location of the parasternal intercostals (P2), and the second location of the sternocleidomastoid (SCM2) will be used as locations for the electrodes.

3.2.3 Experiment 2

The following results were found during the experiment with a COPD patient. The placement of the electrodes on the diaphragm gives the best and most reliable signal of the respiratory muscles during NIV. The AUC from the RMS signal is around twenty times bigger in the diaphragm than in the other two muscles at the start of the measurement with NIV (see Appendix A.5, figure A.7). At the end of the measurement, after an hour of NIV, the diaphragm gives an AUC that is around four times bigger than of the other two muscles (see Appendix A.5, figure A.8). Furthermore, the signal exhibits a strong level of continuity. With the exception of a few breaths, almost every peak in the signal corresponds with the peaks of the airway pressure. In situations where there is airway pressure but the signal is lacking, it may indicate that the patient is being passively ventilated by the NIV system rather than actively initiating their own breaths, this happened more after an hour of NIV than after five minutes. On the other hand, if there is a signal present in the absence of airway pressure, it could be due to motion artifacts.

Although the diaphragm gives the strongest and most reliable signal, the parasternal intercostals seem to be reliable as well. Most of the peaks from the RMS signal correspond with the airway pressure. However, this is less often than the diaphragm (figure 3.3), and the AUC from the parasternal intercostal RMS signal is smaller than that of the diaphragm.

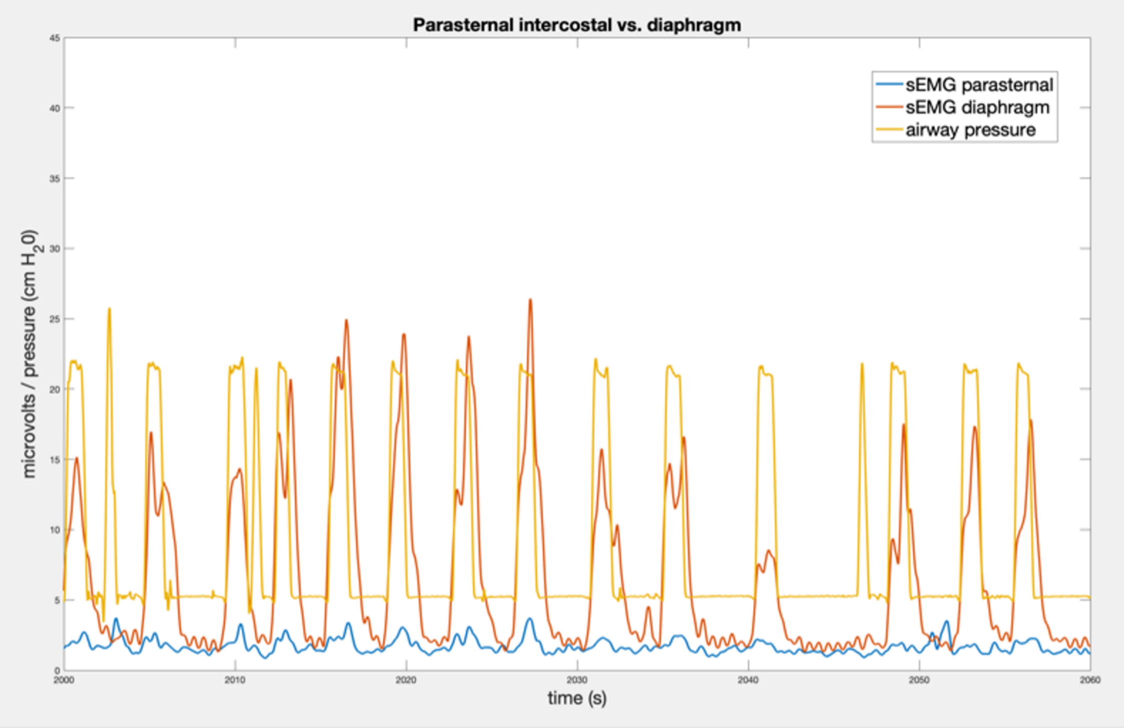

Figure 3.3: *RMS signal from the parasternal intercostal and diaphragm EMG plotted with airway pressure.*

The sternocleidomastoid seems to have the least reliable signal to measure NRD. The signal corresponds with the airway pressure about a quarter of the time, roughly assessed. Besides this, the AUC from the RMS signal is smaller than that of the diaphragm, and around the same amount as the parasternal intercostals. This does not mean that the sternocleidomastoid is not usable to measure the NRD, but, together with the unpleasant feeling of the electrodes in the neck, it is the least preferable of these three muscles.

3.3 Signal interpretation

3.3.1 Noise

The assessed sEMG signals in this study were, in some cases, heavily contaminated with noise. Especially in some parts of the signal from the sternocleidomastoid, where noise made it impossible to distinguish the respiratory rate. However, the signal as a whole was still quite reliable for measuring the NRD. The cause of these disturbances can't be determined with certainty. In this assessment, two main causes of noise are discussed; baseline noise and motion artifacts.

Baseline noise is caused by two intrinsic noise sources that originate in the electronics of the amplification system and the electrode-skin interface, respectively the thermal noise and electrochemical noise [56]. Electrochemical noise is dependent on the gel and skin properties of the patient [57]. Since this experiment used pre-gelled Ag-AgCl electrodes, only the skin properties and preparation of the skin should be taken into consideration for the skin-electrode interface.

The other noise factor is caused by motion artifacts. They can vary widely in their pattern based on the motion they caused, and they could show a great amplitude [56]. In assessing the respiratory patterns, the time intervals with heavy motion artifacts are useless. Although it is likely that there will be motion artifacts when monitoring patients in a nocturnal home setting because the patient can't lay still the whole night, the measurement will be conducted throughout the whole night which should make for time intervals with non-contaminated signals to interpret the data.

3.3.2 Filtering

Several factors should be considered when choosing the right filtering technique. The determination of the bandpass cut-off frequencies is a compromise between reducing noise and artifact contamination on the one hand, and preserving the desired information from the sEMG signal on the other hand.

Burden et al. (2014) tested window lengths of 0.01, 0.15, 0.2, 0.25, and 1 s for mean RMS calculation of EMG signals and concluded that neither statistical significance nor clinical relevance of mean EMG was affected by manipulation of window length [58]. Therefore, the choice of 200 ms envelope was based on the expertise within the CRPH institute of the University of Twente.

The low-pass frequency should be where the amplitude of the noise components surpasses that of the sEMG signal. This means that it is preferable to have a low-pass frequency in the range of 400-450 Hz [56]. The high-pass frequency is more difficult because several noise sources have a low-frequency spectrum that overlaps with the sEMG signal. Especially the fact that the frequency spectra of the ECG and sEMG components strongly overlap makes the complete removal of ECG interference, while maintaining a valid sEMG signal, impossible [58]. To determine the limits of the bandpass filter used for the analysis of the experiments in this study, it was considered that an increase in high-pass frequency reduces the variation in the integrated EMG signal. A literature review resulted in a high-pass filter with a cut-off frequency of 200 Hz, which performed reasonably well in reducing cardiac interference [58].

There are limitations that come with high-pass filtering, such as a decrease in the amplitude of the sEMG signal [59]. However, it remains a strong and simple method in comparison to other techniques. Other techniques like QRS gating mostly guarantees the validity of the remaining signal, but also require discarding a significant fraction of the recorded signal and can't be considered an entirely satisfactory solution either [58]. Another option might be adaptive filtering algorithms, but that requires the measurement of a reference ECG signal, which is impractical in many applications [58].

3.3.3 Ventilation level

NIV can, partly or fully, take over the load of the respiratory muscles. This can reverse fatigue and therefore reduce the NRD to prevent fatigue [60]. The level of ventilation support is important because total unloading is undesirable and increases the risk for ventilator-induced diaphragm atrophy [61]. At the other extreme, inadequate unloading can potentially cause muscle failure and may lead to permanent muscle damage [62].

A high level of unloading results in low activity of the respiratory muscles and therefore a low sEMG signal, this plays an important role in sEMG signal interpretability. As seen in figure 3.4, a breath cycle with total unloading is shown, without diaphragm activity, followed by a triggered breath where sEMG activity can be seen. Consequently, sEMG can provide information about muscle unloading.

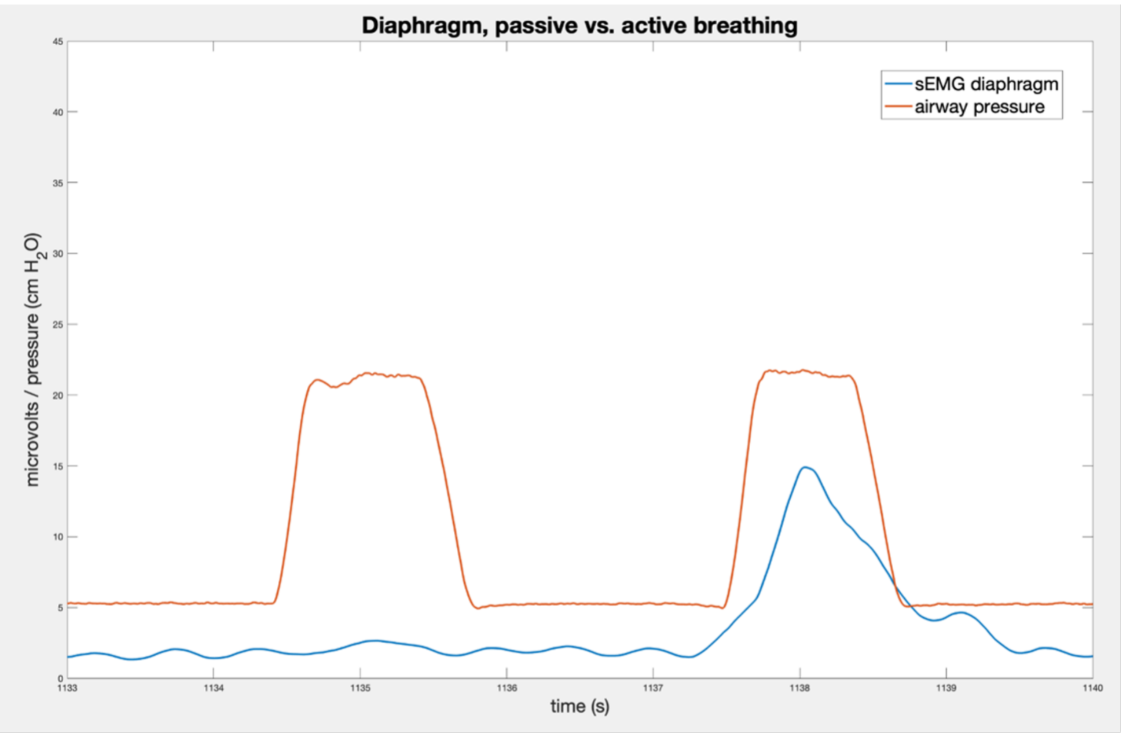

Figure 3.4: *Breath cycle with total unloading followed by breathcycle with partial unloading.*

In the second experiment, five minutes after the start of NIV, the sEMG signal of the diaphragm of three representative breaths were analyzed and showed a mean AUC of 25,9 (see Appendix A.5, figure A.9). The AUC of the signal was measured because it is a more reliable approximation of the NRD than the EMG amplitude. Then, approximately 50 minutes later, three representative breaths were analyzed again and showed a mean AUC of 5,9 (see Appendix A.5, figure A.10). This concludes that in 50 minutes, the NRD decreased by almost 73 percent. Thus, AUC determination of the sEMG signal could be used for assessing NRD progress during NIV.

4 DISCUSSION

The significance of this study is that currently, there is limited knowledge in literature about the use of sEMG with respiratory muscles. Furthermore, the existing knowledge is not specifically focused on the use of sEMG to monitor NH-NIV. This study had the aim to combine all available literature and conduct small-scale tests to explore further possibilities. As a result, it serves as a valuable start for future research.

In this study, certain points were not investigated; however, they should be considered when examining the results and conclusions. Due to time limitations, the researchers chose to prioritize certain aspects. The decision regarding which aspects to exclude was primarily driven by the goal of addressing the broader question of what placement would give a good signal at all, rather than going into the details. Moreover, these excluded points are mostly about aspects where additional literature already exists. Although these points were not extensively examined in this study, they could influence the results or further research, therefore they are pointed out. These points can be divided into two categories; theoretical limitations and practical limitations.

4.1 Theoretical limitations

Some theoretical aspects that need to be taken into account when looking at the study are the interelectrode distance (IED), the difference between sleeping and awake breathing, crosstalk and subcutaneous fat thickness. These points will be explained further below. After an extensive search there was no literature found that investigated the influence of IED on the sEMG signal of respiratory muscles. However, literature on the effect of IEDs in skeletal muscles is known. The main findings were that sEMG signals were not affected by IEDs in healthy subjects [63]. Another article found that the IED did not influence the estimates of normalized RMS in lean subjects while IED differences in obese patients did affect estimates of normalized RMS in the same study [64]. Thus, the subcutaneous fat thickness could influence whether IED is important in assessing EMG signal. Most COPD patients who are classified in the typical chronic bronchitis group tend to be overweight. This results in a higher subcutaneous fat thickness [64]. Therefore, EMG indices for overweight patients could be different. Multiple studies have shown that the lower the subcutaneous tissue thickness, the higher the amplitude and mean frequency estimates [64-66]. In conclusion, further research should be conducted to determine the optimal IED for the respiratory muscles.

Besides this, it should be considered that most studies on nocturnal NIV have not been able to repeat the same positive findings that NIV studies had on lung hyperinflation. One might hypothesize that the daytime awake situation, which is mostly used in research, as compared to sleep could have an influence on the physiology of NIV. For example, being awake, patients might trigger breathing more, have less leakage, less upper airway obstruction, and consequently, larger minute volumes [67].

The last theoretical aspect that needs to be considered is that the electrodes pick up more signal than only the signal of the muscle you want to measure. The main problem with measuring the respiratory muscles is the ECG signal interference, but other muscles can cause crosstalk as well, which is harder or even impossible to filter out [68]. Chiti et al. (2008) concluded that their sEMG signal of the SCM was caused by crosstalk from the scalene since the imEMG of the sternocleidomastoid was silent [27]. However, for the sternocleidomastoid and scalene, it does not matter which exact muscle is measured as long as it measures the NRD correctly. The external parasternal intercostal electrodes pick up crosstalk from the internal intercostals since they overlap [69]. But, because the internal intercostal is active during forced expiration, and the external parasternal intercostal is mostly active during the inspiration, the crosstalk will be minimalized. The diaphragm electrodes are placed on or near the rectus abdominis and internal and external oblique muscles, which makes the diaphragm signal prone to motion artifacts due to the crosstalk from the abdominal muscles. This crosstalk can cause disruption in the measurements of the diaphragm. Consequently, crosstalk needs to be taken into account when examining sEMG signals.

4.2 Practical limitations

During the experiments the researchers conducted, they encountered several practical issues. When considering the various positions of the patient, it is important to take the possibility of movement during the night into account. While efforts could be made to minimize this movement, it is crucial to keep it in mind. The movement can potentially lead to variations in the signal due to the different positions the patient sleeps in. However, since the measurement is conducted throughout the entire night, it is likely that there will still be enough valuable information despite these variations.

When the patient is laying in the lateral decubitus position, attention should be given to the electrodes in the neck. Mainly for comfort and to minimize motion artifacts, it should be determined on which side of the neck the electrodes need to be placed. As mentioned in the research on the position, the electrodes should be placed on the contralateral side of the neck to the side the patient is lying on. This resolves the issues. The only remaining consideration is that the patient should remain on the same side throughout the night. This can be assisted with, for example, pillows that help the patient maintain the correct position. However, the problem remains that if people do not prefer to sleep on their side, this set-up may not be ideal for them.

In the supine position, these problems do not arise. However, it should be considered that the blanket may cause noise due to friction. Also, in the supine position, one should pay attention to the position of the patient's head. For example, if using a very high pillow or an elevated headrest, the patient may be lying at an angle. This could potentially result in increased activation of the abdominal muscles. Although this was not investigated in this study, it is important to keep it in mind and may warrant further exploration.

When looking at the results of the experiment with different ground electrodes and positions, it is important to consider that the measurements were not performed simultaneously. Therefore, slight variations in the signal may occur due to, for example, small differences in position or breathing patterns. The team tried to minimize these variations by performing the measurements with as little time and movement as possible in between. However, it is still necessary to keep the possible presence of small differences in mind.

In the case of the lateral decubitus position, it should be noted that during the experiments, the SCM1 sEMG electrodes were placed on the side of the patient's neck that faced the bed. Surprisingly, this placement exhibited minimal noise on the signal. In the literature review it was found that the contralateral side would be better to prevent too much motion artifacts. However, the experimental results gave different outcomes than anticipated. One possible explanation could be the experimental set-up, where the subject was asked to lay still without a pillow. On the other hand, it was also surprising that the signal from the SCM2, placed contralaterally, had too much noise to distinguish the inspiration. This was also against the hypothesis based on the literature review. It is possible that the position of the electrodes on the neck itself on the bedside may be the cause of these issues, although there could also be other factors involved in the noise. For example, with the placement in the neck, it should be considered that during the experiments the subjects had straws in their mouth to breathe through to simulate COPD breathing. Therefore, it might have been possible that the SCM and scalene were already tightened in order to keep the straw in their mouth.

Upon consideration, this study exhibits both strengths and weaknesses. The most significant strength lies in its exploration of a domain with limited existing knowledge. However, further research is strongly recommended considering the weaknesses of the study. This study serves as a promising stepping stone towards more extensive studies. Ideally, the next research study should consider the aforementioned factors, and particularly, an experiment with a larger study population should be carried out. With further research, the results can be validated and help to eventually establish a standard sEMG protocol for monitoring respiratory activity. Additionally, once positive results have been found, it should be considered to incorporate the monitoring findings into the process of adjusting and personalizing care, using, for example, a feedback loop.

5 CONCLUSION

This study involved a literature review and in-clinic tests on both a COPD patient and lean subjects with simulated respiratory obstruction. The most suitable location of sEMG electrodes on the respiratory muscles in patients with COPD using NH-NIV is on the anterior axillary line, to measure the diaphragm. The placement of the electrodes 3 centimeters either from the midpoint of the sternum or from the sides of the sternum in the second intercostal space is also suitable.

For each patient there are differences in variables such as the IED, subcutaneous fat thickness, sleeping position, ventilation pressure, and breathing type. Because of these differences, the combination of measuring the diaphragm and the parasternal intercostal muscles creates a complete overview of the patient’s muscle activation for respiration in different situations. The advice is to place the sEMG electrodes bilaterally on the anterior axillary line, on the lower costal margin, and 3 centimeters parasternal in the second intercostal space.

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A APPENDIX

A.1 Abbreviation list

COPD: Chronic Obstructive Pulmonary Disease
NIV: Non-invasive ventilation
NH-NIV: Nocturnal home non-invasive ventilation
CHRF: Chronic Hypercapnic Respiratory Failure
sEMG: Surface electromyography
EMG: Electromyography
imEMG: Intra muscular electromyography
teEMG: Transesophageal electromyography
ECG: Electrocardiography
SENIAM: Surface EMG for Non-Invasive Assessment of Muscle
UMCG: Universitair Medisch Centrum Groningen
RMS: Root-mean-square
AUC: Area under the curve
SCM: Sternocleidomastoid muscle
NRD: Neural respiratory drive
RR: Respiratory rate
IED: Interelectrode distance

A.2 Methods search terms

A.2.1 Search terms: Assessing the respiratory muscles for use with sEMG

Search terms included: ‘neural respiratory drive’, ‘COPD’, ‘nocturnal non-invasive ventilation’, ‘NIV’, ‘ventilation’, ‘surface electromyography’, ‘EMG’, ‘inspiratory muscles’, ‘expiratory muscles’, ‘accessory muscles’, ‘muscle activity’, ‘electrode’, ‘diaphragm’, ‘intercostalis interni’, ‘intercostalis externi’, ‘parasternal intercostal, ‘pectoralis major’, ‘serratus anterior’, ‘serratus posterior’, ‘scalene’, ‘sternocleidomastoid’, ‘cleidomastoid’, ‘transversus thoracis’, ‘triangularis sterni’, ‘levator costarum’, ‘subcostalis’, ‘rectus abdominis’, ‘alea nasi’, ‘genioglossus’

A.2.2 Search terms: Determinig the electrode placement per muscle

Search terms included: ‘patient ventilator asynchrony’, ‘neural respiratory drive’, ‘surface electromyography’, ‘intraesophagal electromyography’, ‘EMG’, ‘electrode’, ‘skin’, ‘nocturnal’, ‘non-invasive ventilation’, ‘invasive ventilation’, ‘electric activity’, ‘respiratory onset’, ‘trigger’, ‘pressure support’, ‘COPD’, ‘cystic fibrosis’, ‘signal to noise ratio’, ‘placement’, ‘location’, ‘signal processing’, ‘diaphragm’, ‘parasternal intercostal’, ‘intercostal’, ‘sternocleidomastoid’, ‘cleidomastoid’, ‘scalene’.

A.2.3 Search terms: Signal interpretation

Search terms included: ‘High-pass’, ‘ cut-off frequency’, ‘filtering’, ‘ECG removal’, ‘electrocardiographic interference’, ‘surface electromyography’, ‘adaptive filtering’, ‘EMG’, ‘bandwidth’, ‘respiratory muscles’, ‘artifacts’, ‘ECG’, ‘torso’, ‘noise contamination’, ‘motion artefacts’, ‘baseline noise’, ‘skin-electrode interface’, ‘thermal noise’, ‘respiratory pattern’, ‘skin impedance’

A.3 Experimental protocol 1

Needed supplies
- EMG electrodes 17x: Kendall ECG electrodes from CardinalHealth, H93SG.
- EMG equipment: TMSi porti + laptop that can be connected to the TMSi + USB stick.
- Disinfection wipes
- A straw
- Metronome 30 bpm

Preparation:
- Start the computer.
- Start MATLAB with downloaded TMSi software.

Connecting EMG electrodes:
- Shave and disinfect the skin where the electrodes will be placed.
- Place two electrodes bilaterally on the midclavicular line, on the lower costal margin, called location D1, and place two electrodes on the anterior axillary line on the lower costal margin, one left and one right, called location D2. These are to measure the diaphragm.
- Place two electrodes bilaterally 3 centimeters away from the midpoint of the sternum in the second intercostal space, called location P1, and place two electrodes 3 centimeters away from the sides of the sternum in the second intercostal space, called location P2. These are to measure the parasternal intercostals.
- Place two electrodes with an inner-electrode distance of 1 centimeter on the posterior triangle of the neck on the right side at the level of the cricoid cartilage, called location S1. These are to measure the scalene.
- Place one electrode on the left side of the body on the intersection of the upper one-third and the middle of the sternocleidomastoid and another electrode on the intersection of the lower one third and the middle of the sternocleidomastoid, called location SCM1. Place two electrodes with an inner-electrode distance of 2 centimeters on the right sternal head of the sternocleidomastoid, called location SCM2.
- Place one electrode on the sternum, one on the middle point of the clavicula and one electrode on the styloid process at the head of the ulna. These will function as common electrodes.
- Connect the wires of the TMSi to the electrodes. Number 1 (P1) and 2 (P2) for the parasternal intercostals (red right, black left), numbers 3 (D1) and 4 (D2) for the diaphragm (red right, black left), number 5 (S1) for the scalene (red top, black bottom) and numbers 6 (SCM1) and 7 (SCM2) for the sternocleidomastoid (red top, black bottom).
- The common electrode wire should be connected to either the sternum, clavicula or wrist:
o For experiments 1, 4 and 7, place the common electrode on the sternum.
o For experiments 2 and 5, place the common electrode on the clavicula.
o For experiments 3 and 6, place the common electrode on the wrist.

Tests of the EMG:
- Experiments 1, 2, 3, and 7 are measured while the participant is laying on their back.
- Experiments 4, 5 and 6 are measured while the participant is laying on their left side.

Experiments 1-6:
- Start a metronome of 30 beats per minute.
- Let the participant breathe in and out on the beeps of the metronome, maintaining a respiratory rate of 15 breaths per minute.
- Let the participant breathe through one straw for 2,5 minutes.
- After 30 seconds of breathing in the straw, start example04.m of the TMSi software in MATLAB
- After 2 minutes of measurements, stop example04.m. A Poly5 document will be created.
- Rename the Poly5 document according to the experiments conducted.

Experiment 7:

- Start a metronome of 30 beats per minute.
- Let the participant breathe in and out on the beeps of the metronome, maintaining a frequency of 15 breaths per minute.
- Start example04.m of the TMSi software in MATLAB.
- After one minute of measuring, let the participant breathe through one straw for another minute.
- After measuring for a total of two minutes, stop example04.m. A Poly5 document will be created.
- Rename the Poly5 document according to the experiments conducted.

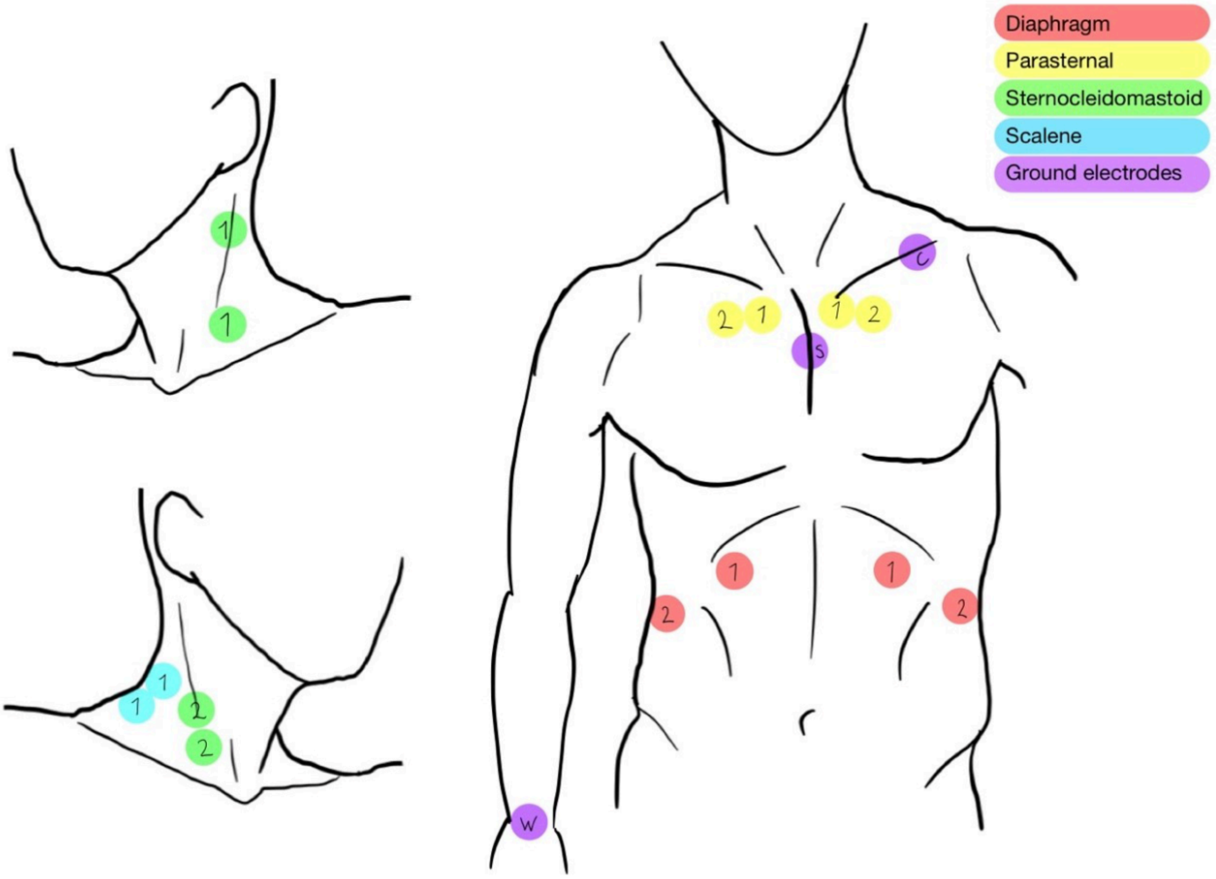

Figure A.1: *Experimental setup experiment 1*

A.4 Experimental protocol 2

Needed supplies:
- EMG electrodes 7x: Kendall ECG electrodes from CardinalHealth
- EMG equipment: a laptop that can be connected to the Dipha, the Dipha + USB stick.
- Disinfection wipes

Preparation:
- Start up the computer.
- Start Polybench Data Manager and insert the USB of the Dipha into the computer.
- Create a new patient under the name (TGO-groep18), so that no data can be deduced back to the patient!

Connecting EMG electrodes:
- Clean the skin with an alcohol wipe on the areas where the electrodes are applied.
- Place an EMG patch on the manubrium sterni, which serves as the ground electrode.
- Apply two EMG patches to the second intercostal space on both sides, approximately 3 cm parasternally, to measure the intercostal muscles 1.
- Place two EMG electrodes bilaterally approximately 3cm parasternal in the second intercostal space to measure the parasternal intercostals.
- Place two EMG electrodes on the right anterior axillary line and the left anterior axillary line on the costal arch to measure the diaphragm.
- Place two EMG electrodes on the right sternal head of the sternocleidomastoid, with 1 centimeter distance between the electrodes.
- Connect the wires to the EMG electrodes: number 1 and 2 for the electrodes measuring the parasternal intercostals. Wires 3 and 4 for the diaphragm. Wires 5 and 6 for the SCM. And the black wire for the ground electrode on the sternum.
- Place the pressure measurement adapter between the tubing and the mask. Place the end of the intermediate piece (green hose) in the pressure gauge of the Dipha, and take the hose with number 1. (if this does not work, try the other hoses)

Tests of the EMG:
- Click the two orange boxes of the Dipha together until you hear a click, there is a beep and a green light starts to burn.
- Check that the correct patient is selected on the left side of the screen.
- Click on the correct measurement functionality on the right side of the screen: sEMG-8-Elec-1Pressure-Dipha180001. You will now enter a new screen.
- Check the screen at the top right if the Dipha Device is selected correctly: this should be Dipha120032.
- You should now see twelve signals on the right side of the screen.
- Click on Start on the right side of the screen and check that these are good signals and that all electrodes are working properly.
- Check if the pressure is measured correctly by blowing briefly into the intermediate piece.
- If everything works properly, ask the patient to perform several situations.
o Start with breathing normally without the mask in supine position.
o Breathing normally with the breathing mask in supine position.
o Try to sleep in a comfortable position (either supine or lateral decubitus) with the mask.
o Breathing normally in the position opposite to the position the patient slept in.
- Insert marks as follows:
o M1 to start and stop the baseline measurement.
o M2 to start and stop the main measurement.
o M4 to start and stop the after-sleeping measurement.
- Stop the measurement again by clicking on Home and then on stop and Exit.

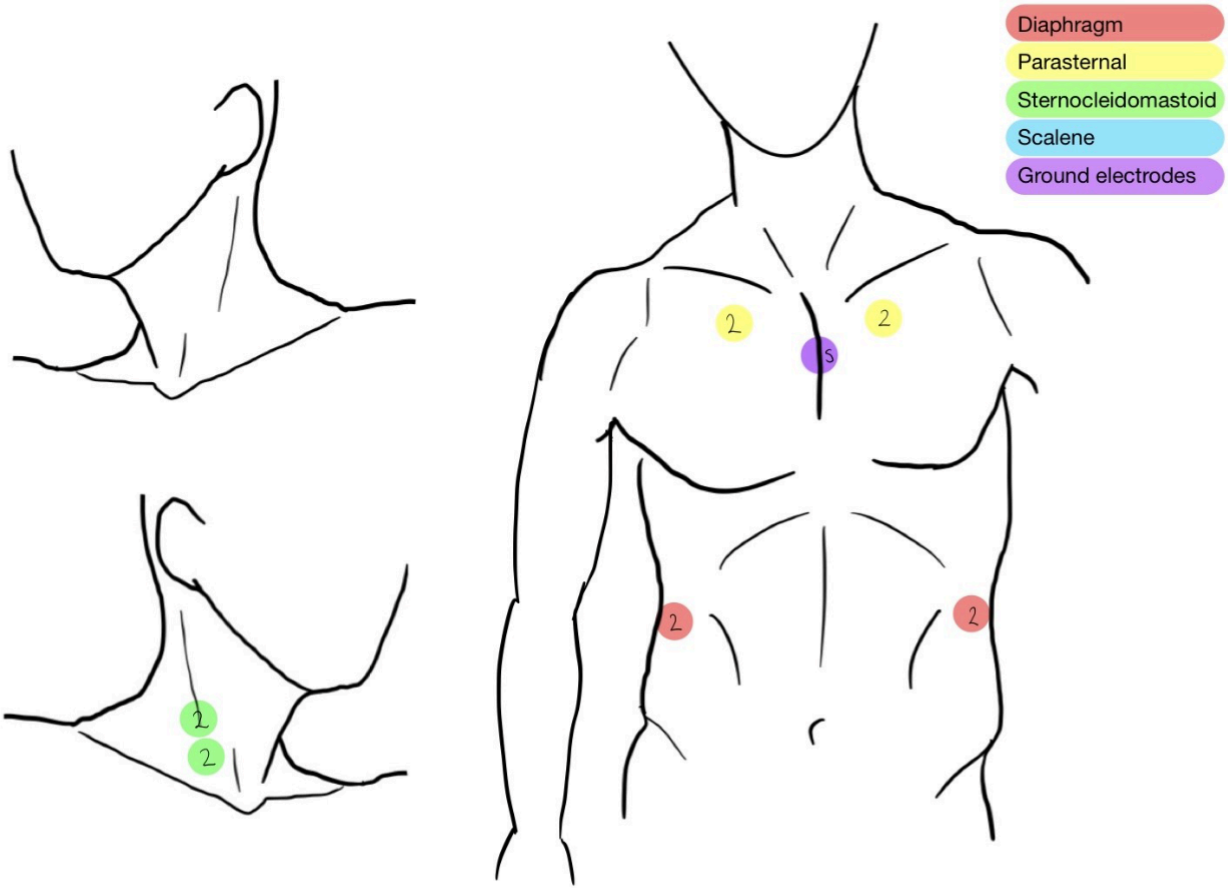

Figure A.2: *Experimental setup experiment 2*

A.5 Graphs

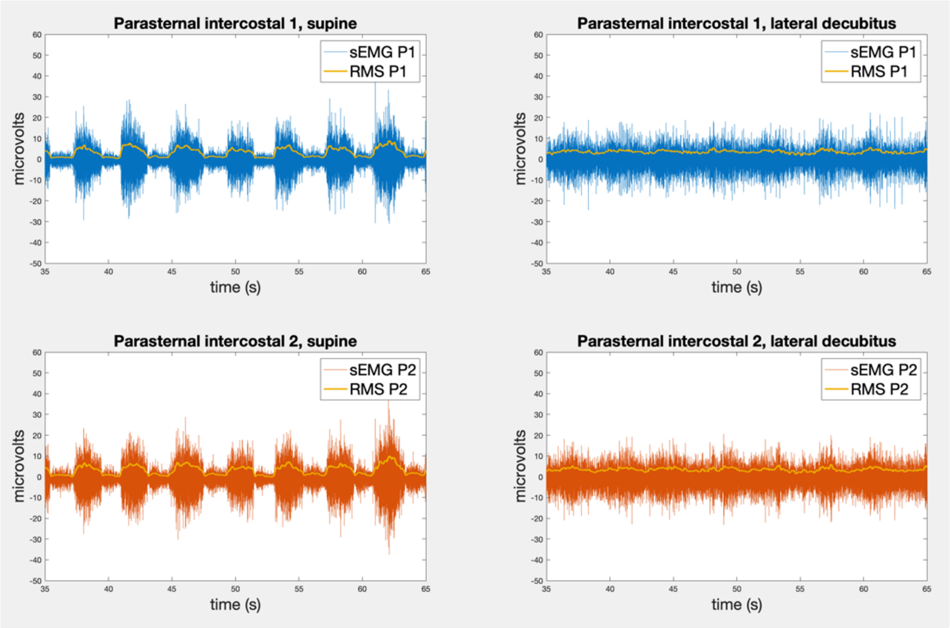

Figure A.3: *EMG signals from P1 (top) and P2 (bottom) electrode placements on the parasternal intercostal muscles, in supine (left) and lateral decubitus (right) position.*

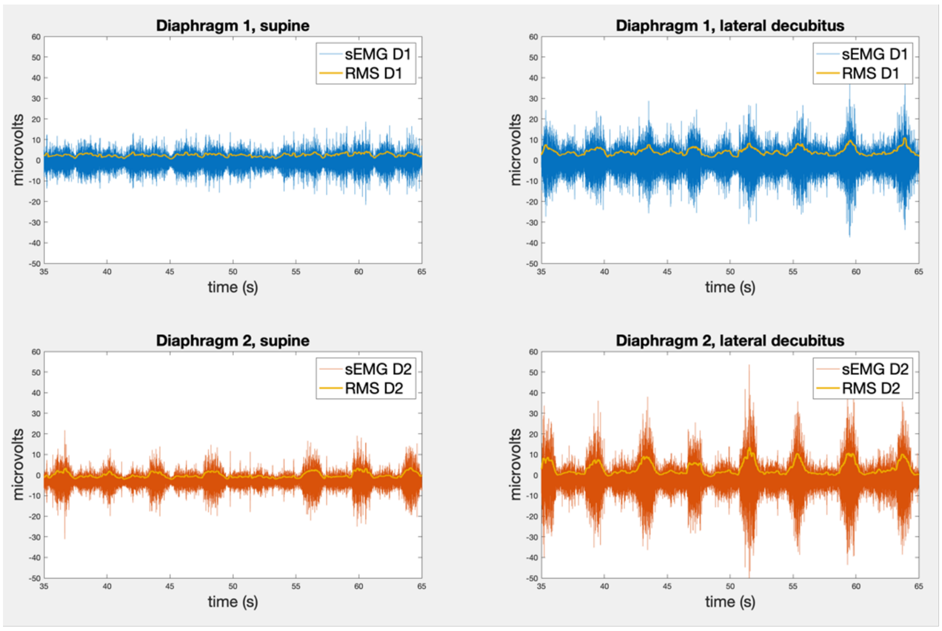

Figure A.4: *EMG signals from D1 (top) and D2 (bottom) electrode placements on the diaphragm, in supine (left) and lateral decubitus (right) position.*

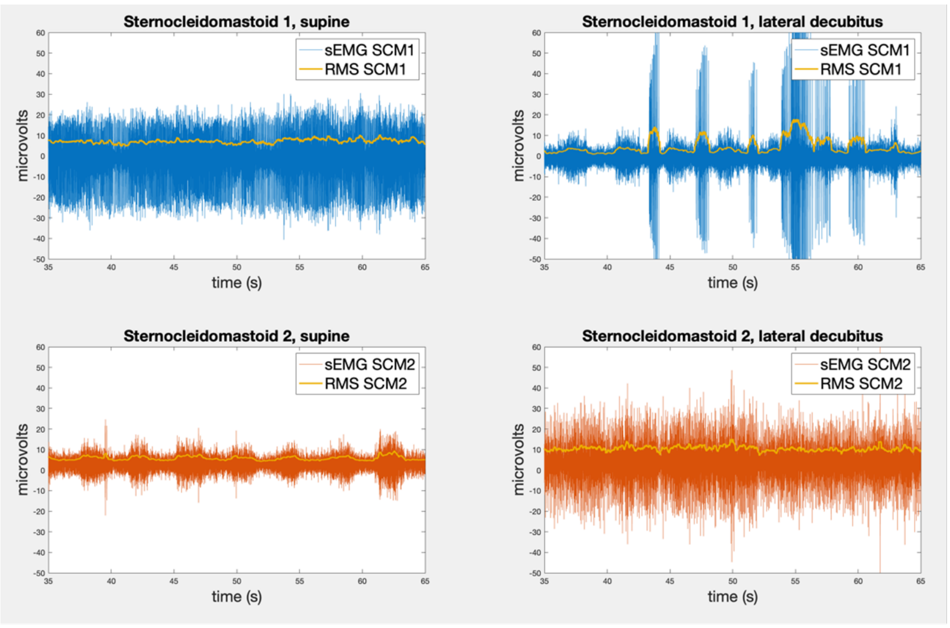

Figure A.5: *EMG signals from SCM1 (top) and SCM2 (bottom) electrode placements on the sternocleidomastoid in supine (left) and lateral decubitus (right) position.*

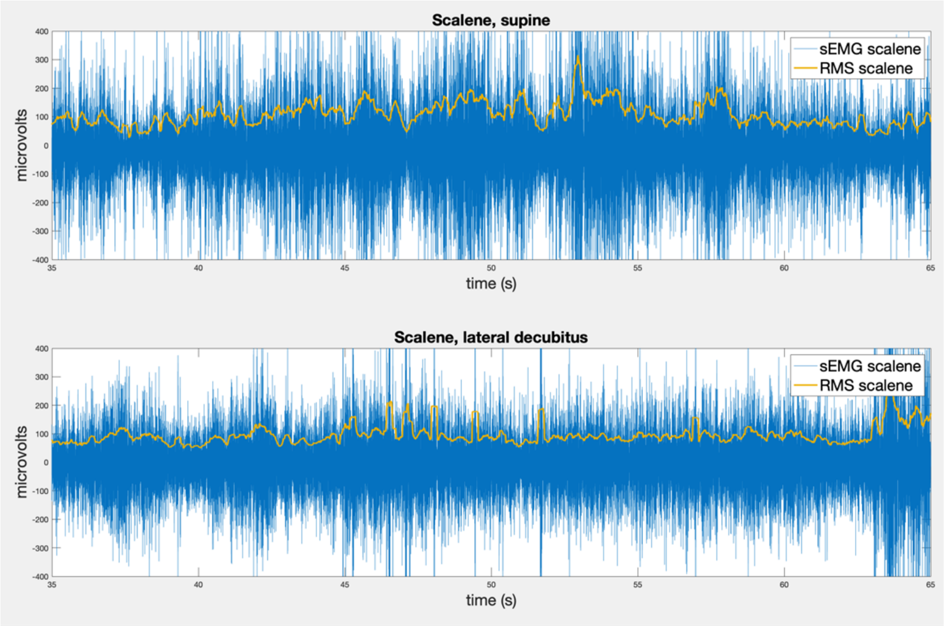

Figure A.6: *EMG signals from the electrode placement on the scalene, in supine (top) and lateral decubitus (right) position.*

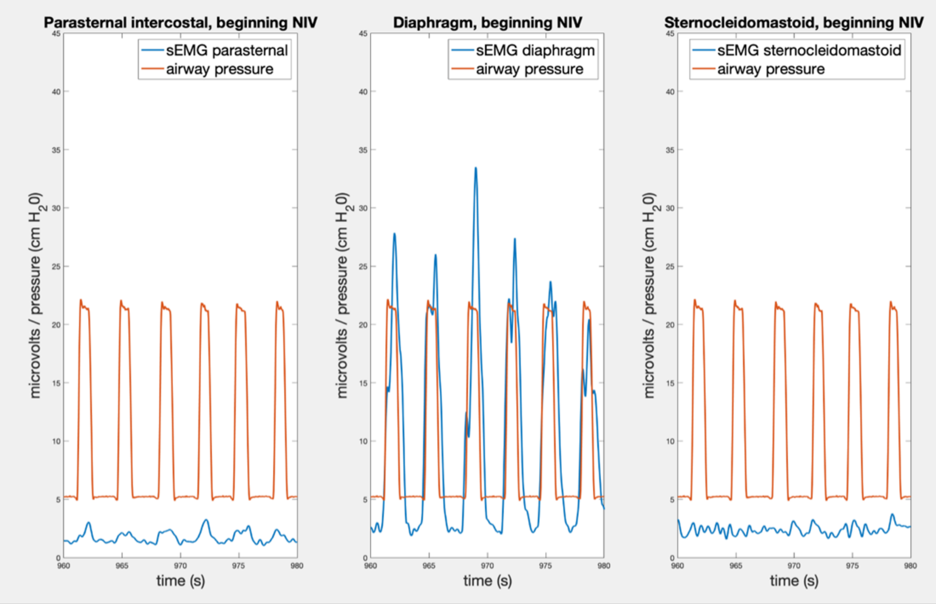

Figure A.7: *Airway pressure together with EMG RMS signal of parasternal intercostal muscles (left) with an AUC of 1.4, diaphragm (middle) with an AUC of 24.5, and sternocleidomastoid (right) with an AUC of 0.9 after five minutes of NIV.*

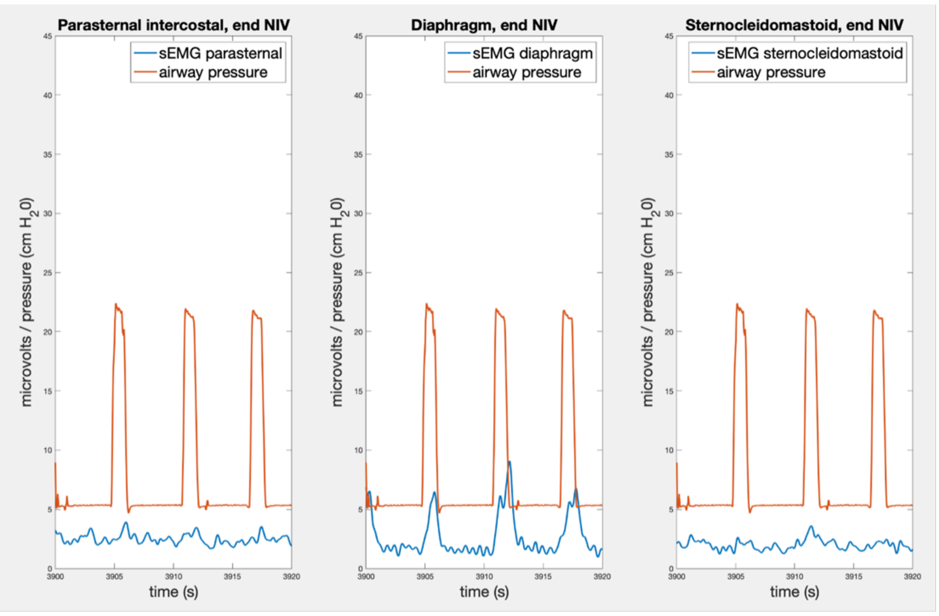

Figure A.8: *Airway pressure together with EMG RMS signal of parasternal intercostal muscles (left) with an AUC of 1.5, diaphragm (middle) with an AUC of 6.2, and sternocleidomastoid (right) with an AUC of 1.5 after an hour of NIV.*

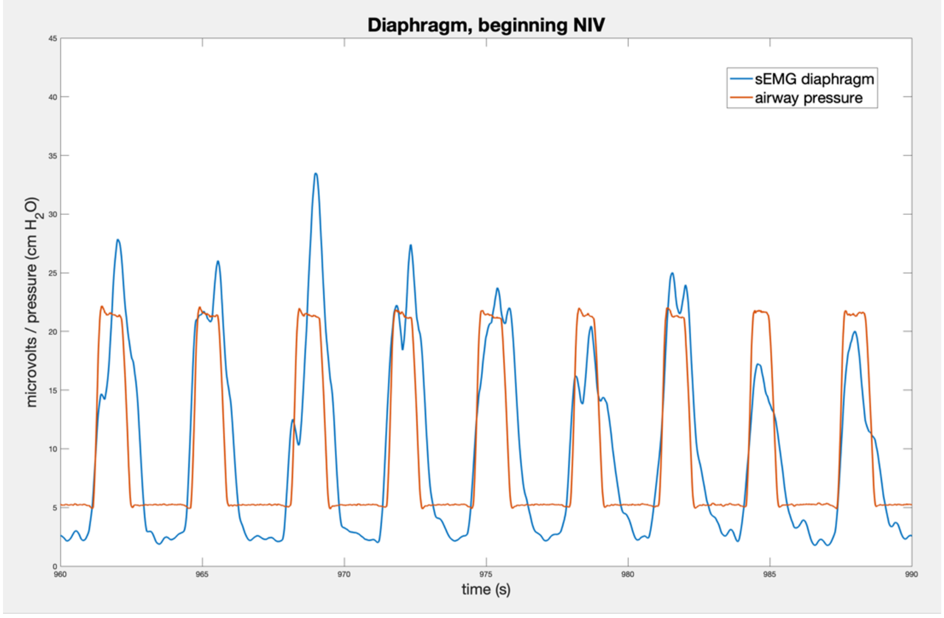

Figure A.9: *Airway pressure together with EMG RMS signal of the diaphragm with a mean AUC of 24.5 after five minutes of NIV*

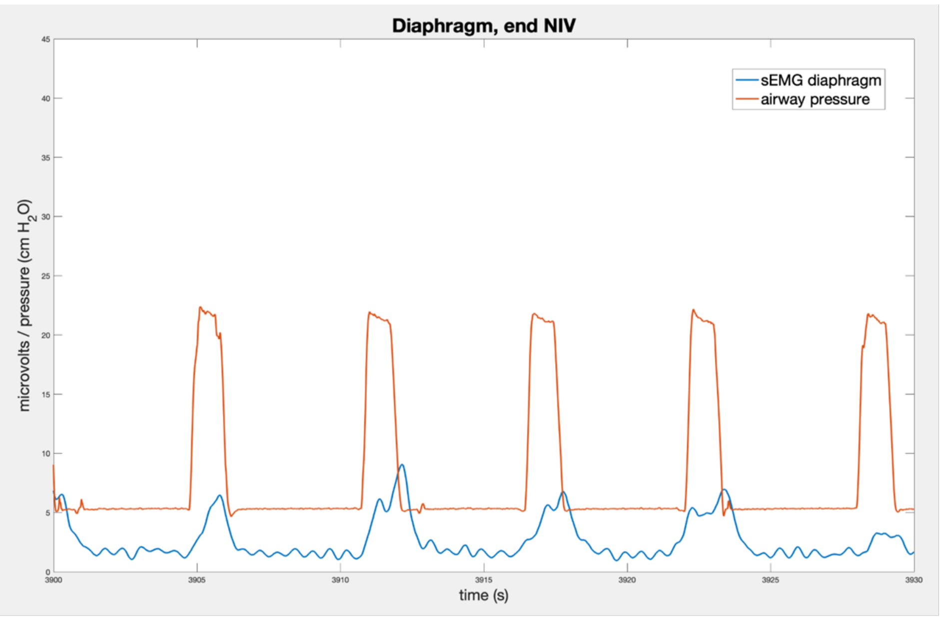

Figure A.10: *Airway pressure together with EMG RMS signal of the diaphragm with a mean AUC of 6.2 after an hour of NIV.*