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Using a Sniff-Controller to Self-Trigger Abdominal Functional Electrical Stimulation for Assisted Coughing Following Cervical Spinal Cord Lesions

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***Abstract*— Individuals with cervical spinal cord lesions (SCL) typically depend on caregivers to manually assist in coughing by pressing against their abdominal wall. Coughing can also be assisted by functional electric stimulation (FES) applied to abdominal muscles via surface electrodes. Efficacy of FES, however, depends on precise temporal synchronization. The sniff-controller is a trigger that enables paralyzed individuals to precisely control external devices through alterations in nasal airflow. We hypothesized that FES self-triggering by sniff-controller may allow for effective cough timing. After optimizing parameters in 16 able-bodied subjects, we measured peak expiratory flow (PEF) in 14 subjects with SCL who coughed with or without assistance. Assistance was either manual assistance of a caregiver, caregiver activated FES, button self-activated FES (for SCL participants who could press a button), or sniff-controlled self-activated FES. We found that all assisted methods provided equally effective improvements, increasing PEF on average by 25 ± 27% ($F[4,52]=7.99$, $p=0.00004$). There was no difference in efficacy between methods of assistance ($F[3,39]=0.41$, $p=0.75$). Notably, sniff-controlled FES was the only method of those tested that can be activated by all paralyzed patients alone. This provides for added independence that is a critical factor in quality of life following SCL.**

***Index Terms*— Assistive technology, cough, functional electrical stimulation (FES), sniff-controller, spinal cord lesion (SCL).**

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I. INTRODUCTION

THERE are between 250,000 and 500,000 new cases of spinal cord lesions (SCLs) worldwide annually. SCLs are associated with an elevated risk of death, mostly during the first year after lesion [1]. Different secondary conditions, such as pneumonia, pressure ulcers and urinary tract infections are a major cause of morbidity and mortality following SCL [2, 3]. These conditions frequently lead to hospitalization and can also result in increased costs of care, reduced employability, decreased quality of life and lowered life expectancy [1, 2, 4-6]. Respiratory complications, which are among the major causes of morbidity and mortality after SCL, may occur in patients with lower cervical or high thoracic SCL. These complications occur in part because of paralysis of the abdominal muscles, which are required for expiration in the upright position, support effective inspiration, [7, 8] and enable coughing. Coughing is necessary for efficient removal of secretions and solid particles from the respiratory tracts [9]. Impairment of coughing may cause bronchial obstruction and consequent atelectasis pneumonia with severe respiratory disturbances [7]. Therefore, when abdominal muscles are paralyzed, external assistance is required for coughing. At present, an individual with SCL who needs assistance for coughing frequently depends on a caregiver applying intermittent manual pressure to the anterior abdominal wall [10, 11].

To minimize dependency on a caregiver, individuals with SCL frequently use assistive technologies. They may need assistive technology just after injury, or throughout life. The level of the SCL and associated impairments, environmental factors, personal factors and comorbid health conditions influence the type of required assistive technology. Assistive technologies can include mobility devices, communication devices, aids for self-care, and aids for domestic activities and environmental control systems that help in daily function [1]. In the case of coughing, there are several available assistive technologies: These include manual air stacking, or glossopharyngeal breathing (GPB), where the patient basically gulps boluses of air to later be expired as a cough. These gulps

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of air can be self-generated or manually assisted [12, 13]. Air stacking depends on an intact glottis, and if this fails an added one-way flow valve type device can compensate for air leakage [14]. Additionally, small manual devices that combine high-frequency airflow oscillations with positive expiratory pressure (PEP) can be used to assist in coughing [15]. In turn, several approaches can be used to externally activate abdominal muscles, one of which is functional electric stimulation (FES) applied to abdominal muscles [8, 16-21]. This method, however, is not always effective, possibly due to the lack of synchronization accuracy in FES triggering. In coughing, afferent impulses of the cough reflex processed by the brain-stem cause a series of synchronized events in the following order: (I) air inspiration; (II) tight closure of the glottis and vocal cords to trap the air within the lungs; (III) forceful contraction of abdominal muscles and accessory expiratory muscles to increase air pressure within the lungs; and (IV) sudden opening of the vocal cords to enable the immediate forceful blowing out of air with secretions and solid particles [22]. This series of events requires precise synchronization in order to evoke an effective cough, and the timing of its activation by FES is critical for the synchronization between glottis closure and abdominal muscle contraction.

Several previous studies reported FES triggering using physiological measures. These included electromyographic (EMG) signals from either the pectoralis major muscle or the deltoid muscle [20], as well as various measures of respiration [23-28] (more on this in the discussion). Here we set out to investigate a novel alternative for FES control, namely the sniff-controller. The sniff-controller detects slight perturbations in nasal airflow and converts these into electrical signals that can control external devices [29]. Because nasal airflow is modulated in part by the soft palate [30], which is innervated by cranial nerves [31, 32], the sniff-controller remains functional following any type of SCL [29]. The sniff-controller can be programmed to control a host of assistive technologies ranging from mobility to communication. Its application to FES triggering may be particularly appropriate because sniff-controller activation and cough mechanisms likely rely on common neural substrates of respiration. For example, c-Fos studies in cats have identified several brainstem structures involved in both sniff and cough [33, 34]. These include the nuclei of the solitary tract, the lateral reticular nucleus, the medullar raphe nuclei, and the parabrachial and Kölliker-Fuse nuclei of the pons [33, 34]. Moreover, several lines of evidence imply a critical role for the Bötzinger complex in both sniffing [35] and coughing [36]. With this in mind, we set out to optimize FES triggering by sniff-controller in able-bodied subjects, and then applied this optimized system in individuals with SCL, where we compared its performance to non-assisted and assisted coughing.

II. METHODS

A. Subjects

We approached current and past patients of the Loewenstein rehabilitation hospital. Inclusion criteria were: Tetraplegic men and women aged 20 to 60 years, with complete low cervical or high thoracic SCL (ASIA grade A or B) with motor impairment related to segments C4-T6. Exclusion criteria were: Respiratory difficulties not directly related to the spinal injury; Pacemaker; Electronic implant; Pressure wound; Pregnancy; Inability to communicate with the experimenter. For able-bodied participants we applied the same exclusion criteria. These criteria yielded 16 able-bodied subjects (4 women, age: 25-44 years) and 14 subjects with low cervical or high thoracic SCL (2 women, age: 21-57 years) who all participated in the study after providing informed consent to procedures approved by the Helsinki Committee of Loewenstein Rehabilitation Hospital. Notably, some of the patients had sporadically experienced FES long before this study, but none of them were regular users. Additional details on participants with SCL are available in Table I.

Subject	Injury Level	ASIA Grade	Time From Injury (Years)	Gender	Age
1	C6	C	3	M	35
2	T2	A	15	M	42
3	C4	A	10	M	56
4	T4	A	6	M	33
5	T4	A	5	M	47
6	C5	A	7	M	37
7	T4	A	3	M	41
8	T4	A	37	M	57
9	C4	A	11	M	48
10	C6	A	8	M	35
11	C5	B	17	M	50
12	C5	A	9	F	21
13	C6	A	2	M	24
14	C5	B	10	F	29

Fourteen participants with SCL, detailing level of spinal injury, ASIA grade, time from in years, gender and age.

B. Characterizing Nasal Airflow During Cough Events

Our aim was to mimic the natural cough reflex. This includes precise synchronization of abdominal muscle contraction and progressive glottis closure. We therefore conducted experiments designed to characterize the temporal relation of these events with nasal airflow and muscle activity in the anterior neck and abdomen. To this end we developed an experimental setup that included an endoscopic video camera (Portable Bedside Laryngoscope, Distal Tip 3.4 mm, PENTAX) that was synchronized with nasal airflow measurement, a microphone, and a signal amplifier (ETH-256, iWorx Systems, Inc.) for EMG of the anterior neck and abdominal muscles as illustrated in Fig. 1. For measuring airflow we used a nasal cannula linked to a sniff controller device [29]. Data was recorded using an instrumentation amplifier (ADInstruments PowerLab 8SP) at 1 kHz and LabChart 7 for Mac software (ADInstruments). Note that this

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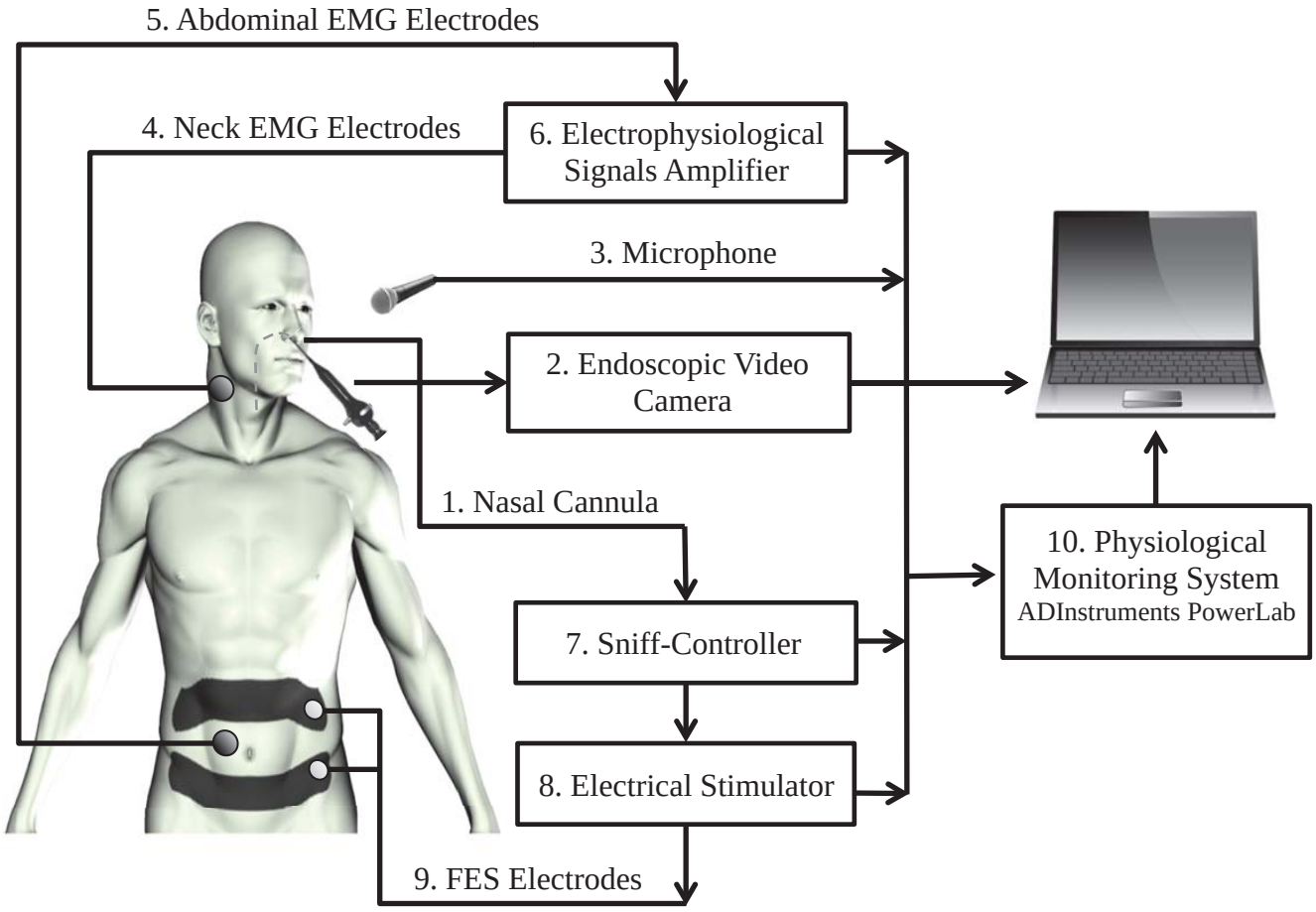

Fig. 1. The experimental apparatus used in able-bodied participants. We obtained simultaneous measurements during coughing from: 1. Nasal cannula, 2. Endoscopic video camera, 3. Microphone, 4. Neck EMG, 5. Abdominal EMG, 6. Electrophysiological Signals Amplifier 7. Sniff-Controller, 8. Electrical stimulator, 9. FES electrodes. We placed electrodes in two rows. Each row contained four electrodes connected to a single pole of the stimulator. This made for effectively two large stimulating electrodes as illustrated. 10. Physiological monitoring system (ADInstruments Powerlab).

setup with video camera and EMG was applied in the able-bodied subjects only.

C. Integration of the Sniff Controller with FES

The system used for computerized control of the FES incorporated the sniff controller technology that included an Arduino microcontroller device (www.arduino.org). The microcontroller received analog inputs from the airflow sensors and was programmed to trigger the FES. This system can switch between manual and self-activation modes using a standby button. The standby status can be set in place using a sniff-controller command. After defining the features of the nasal respiration pattern that indicate the progressive glottis closure, we developed software that continuously samples the sniff trace and detects the defined features. This software is here made publically available in the Supplementary Materials (note that instructions for construction of a complete sniff-controller have also been made publically available at http://www.snifflogic.org/#!diy such that the entire device described in this manuscript can be constructed with relative ease).

D. FES Experimental Setup

Stimulation was delivered by Constant Current Stimulator (DS7A, Digitimer), using self-adhesive surface electrodes [Size 5 cm x 13 cm, Model 895250, AXELGAARD) directly over the abdominal muscles of SCL subjects lying in the supine position. A constant current of 240 mA (0.92 mA/cm2) was delivered for 500 ms, which consisted a train of 200 μs monophasic square pulses at 100 Hz. Given that the effectiveness of FES increases with stimulus intensity and plateaus at ~211 mA [37], our selection of 240 mA puts us well within this optimal range. FES is often applied bilaterally using four separate electrode pairs [23]. In the present study we used a different configuration of stimulating electrodes (Fig. 1): Four self-adhesive surface electrodes were situated in a row next to each other on the abdominal muscles above the umbilicus, and were connected in parallel to one output pole of the stimulator. Similarly, another set of four electrodes was situated under the umbilicus, and was connected the other output pole. This effectively constituted two large stimulating electrodes (260 cm2 each) aimed at maximizing the stimulated area.

E. Cough Efficacy Experiments

We tested cough efficacy comparing five different methods for cough induction: 1. Without assistance. 2. With manually

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assisted expiration (by a physiotherapist). 3. FES-assisted expiration activated by a caregiver. 4. Button-press self activated FES-assisted expiration. 5. Sniff-Controller-FES automatic activation. To assess the effects of the different methods for increasing the intra-abdominal pressure during cough and breathing we measured peak expiratory flow (PEF) during cough. In other words, PEF was the measure of cough efficacy in this study. We also measured forced vital capacity (FVC), and maximal voluntary ventilation (MVV) after cough. Lung functions after cough were measured in the supine position and with nostrils sealed by nasal clips, using a Pony FX device and Omnia 1.2 (COSMED, Italy) software. The participants were encouraged to achieve maximal capacity in the respiratory tests, and the best of three attempts was included in the analysis. The order of tests was sequenced randomly.

F. Statistical Analyses

The modes of cough (assistance and its types) were submitted to a within-subjects repeated-measures analyses of variance (ANOVA) followed by planned comparisons with t-tests for each variable (PEF, FVC, MVV). Data were analyzed using STATISTICA for Windows (version 7.0; StatSoft, Inc., Tulsa, OK, USA). The use of within-subjects tests minimized any impact of individual differences in extent of injury and impairment.

III. RESULTS

A. Identifying the Sniff-Controller Time Point for FES Activation

To characterize the pattern of nasal respiration during cough we first tested eight able-bodied subjects who were asked to breathe through their nose and cough spontaneously. We recorded the progressive events that involve coughing, as shown in Fig. 2. Respiration airflow rates higher and lower than baseline correspond to inspiration and expiration, respectively. The cough sequence is characterized by higher peak flow compared to the prior inhalation (Fig. 2), which is the first event of the cough process. The second event is tight closure of the glottis to trap air within the lungs. The initiation of glottis closure is associated with a rapid decrease of the inspiration flow rate towards zero or baseline, followed by a relatively small local peak of expiration flow rate (as marked by left circle in Fig. 2). This peak, observed in 98% of cases, can be related to measured pressure vibrations resulting from the rapid complete closure of the glottis. Examination of the endoscopic video synchronized with nasal airflow measurement suggested that glottis closure begins with vocal cord shutting followed by progressive contraction of the glottis spanning several milliseconds. The mean time difference between the visualized glottis closure and the following local minimum of respiration flow rate was 45 ± 40 ms (Fig. 3 and Online Video). During the third event, which is a spontaneous forceful contraction of abdominal muscles and accessory expiratory muscles, the glottis remained closed. Thus, airflow is halted and as expected, we observed a plateau of the respiration flow rate, until opening of the glottis. We found that the mean glottis closure duration was 411 ± 218 ms. The last event in the cough process, a sudden opening of the glottis and vocal cords and outward expulsion of the air under pressure, is clearly evidenced in the sniff trace.

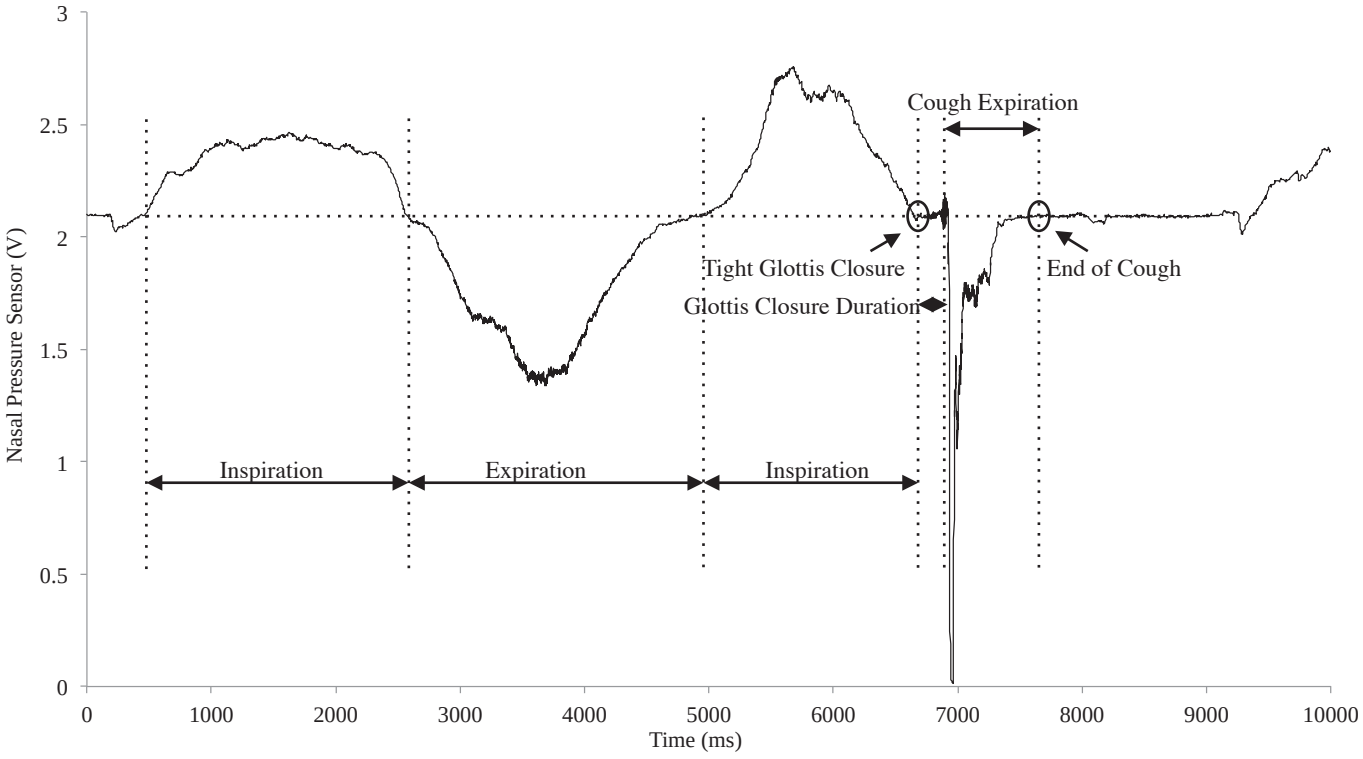

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Fig. 2. Nasal respiratory pattern during progressive cough events in an able-bodied subject. The ordinate is signal from the sniff-controller reflecting nasal airflow (converted into volts). The dotted horizontal line reflects baseline, or the point of shift between inhalation and exhalation. Individual events such as glottis closure were obtained through simultaneous endoscopic video.

The above parameters were identified during normal breathing that is predominantly nasal. To estimate the value of the residual nasal signal evident during oral breathing we again tested the system in eight able-bodied subjects who were asked to breathe through the mouth and cough voluntarily.

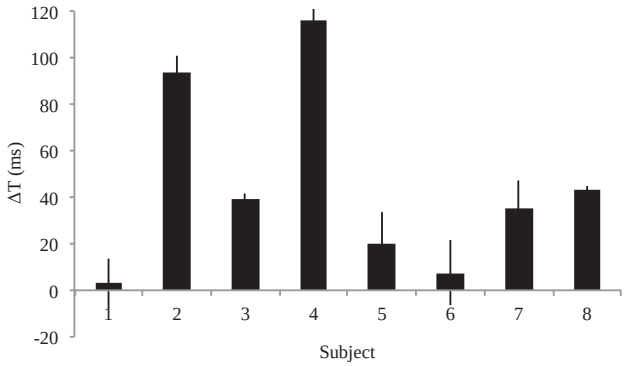

Fig. 3. Time difference (ΔT) between glottis closure and respiration minima. The ordinate is time difference in milliseconds and the abscissa is subject serial number. Bars are SE.

We observed that nasal respiration was idiosyncratic for each individual and the dynamics of the soft palate were changed during the experiment. This was reflected by differentiation of the inhalation peak, the negative slope rate, the local minimum of the flow rate and glottis closure duration. Nevertheless, the sniff-controller continuously measured airflow during cough, detected the timing of glottis closure (the local minimum of the flow rate of respiration) and emitted a FES-activation signal with a pre-defined delay (50 ms) (Fig. 4) (note that FES stimulation was not delivered to the able-bodied subjects). In other words, the system synchronized cough detection and FES activation at the time frame of natural coughing even when respiration was not intentionally nasal. As cough was detected, the sniff-controlled device activated the stimulator to elicit a pulse train at a frequency of 100 Hz for 500 ms, with a pre-determined delay after the minimum time-point. The system response was highly accurate; the mean delayed time of FES triggering was 36 ± 8 ms, which was immediately followed by stimulator output (Fig. 4). The mean duration of the glottis closure was 411 ± 218 ms in subjects that were asked to breath regularly (mostly nasaly), and cough voluntarily, but only 187 ± 83 ms in those who were asked to breath through the mouth and cough. Inhalation was deeper before cough in 91% of the cases, higher than the previous inhalation by 10 ± 5%.

B. Activity of Neck and Abdominal Muscles During Cough

We recorded EMG signals from abdominal and neck muscles during cough in eight able-bodied subjects. We found that the abdominal muscle contraction was a progressive process that on average remained active for 559 ± 310 ms.

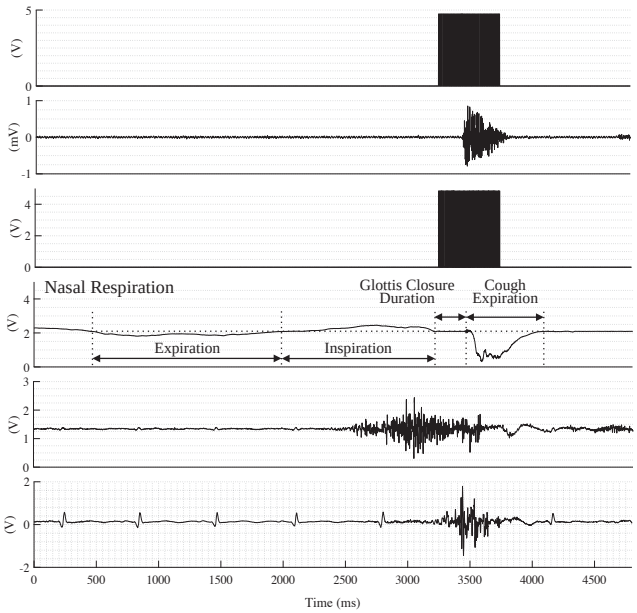

Fig. 4. Timeline of experimental events. Experimental measurements of nasal respiratory pattern synchronized with sound recording and EMG of neck and abdominal muscles in an able-bodied subject.

Activity started 174 ± 275 ms before glottis closure, and in 30% of the cases it was also observed after glottis closure (Fig. 4). Furthermore, neck muscle activity started before abdominal muscle activity, and 415 ± 240 ms before the onset of minimal airflow, and in total lasted together with glottis muscle activity for 826 ± 347 ms.

C. Cough Efficacy of Assistive Methods

Fourteen subjects with SCL participated in this part of the study. Once the sniff-controller was put in stand-by mode (this can be done by a key-board command or by a sniff-controller command, e.g., sniff in-out-in within one second), it triggered FES activation based on the above results. Specifically, given the above-observed difference of 45 ± 40 ms between the airflow minima and full glottis closure, the trigger was activated 50 ms after airflow minima. We then individually fine-tuned the delay, based on patient self-report of cough efficacy during 3-5 test-coughs. This resulted in an average delay of 152 ± 70 ms, which is 67% ± 20% of the glottis closure duration (The delay time was normalized according to glottis closure duration for each subject). Three subjects retained the unoptimized 50 ms window. An ANOVA on PEF values during cough with conditions of assistance (assisted/unassisted) and mode (caregiver/caregiver-FES/self-FES/sniff controller) revealed a main effect of assistance ($F[4,52] = 7.99$, $p = 0.00004$), and no effect of mode ($F[3,39] = 0.41$, $p = 0.75$). Planned comparisons revealed that this reflected a significant increase in PEF with assistance, but no difference between assistive methods (mean PEF unassisted =

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5.42 ± 1.55 L/s, mean PEF caregiver = 6.77 ± 1.93 L/s, mean PEF caregiver-FES = 6.60 ± 1.79 L/s, mean PEF self-FES = 6.83 ± 2.01 L/s, mean PEF sniff controller = 6.57 ± 1.94 L/s, all comparisons with unassisted cough $t(13) > -4.01$, $p < 0.0015$, all comparisons between methods of assistance $t(13) < 1.15$, $p > 0.27$ (Table II , Fig. 5). The mean PEF of automatic Sniff-Controller-FES assisted cough was 23 ± 27% higher than coughing without assistance, and subjects self reported that the automatically stimulated cough was highly effective, and did not cause any discomfort. The mean FVC and MVV values after cough were 3.01 ±0.11 L and 70.89 ±6.57 L/min (3.5% and 9.3%), respectively. The methods of coughing did not affect MVV ($F[4,48] = 0.30$, $p = 0.89$), and the effect on FVC was marginal ($F[4,52] = 2.54$, $p = 0.051$).

TABLE II
COUGH EFFICACY OF ASSISTIVE METHODS

Subject	PEF [L/s]	PEF Ratio Assistive/Unassistive	Time Ratio Trigger Onset/Glottis Closure Duration
No assistance	5.42 ± 1.55	-	-
Caregiver	6.77 ± 1.93	1.28 ± 0.28	-
Caregiver-FES	6.60 ± 1.79	1.25 ± 0.25	0.33 ± 0.53
Manually Self-FES	6.83 ± 2.01	1.26 ± 0.28	0.78 ± 0.26
Auto Sniff Controller-FES	6.57 ± 1.94	1.23 ± 0.27	0.67 ± 0.20

The five methods of coughing tested in this study, and the associated PEF values with each (mean ± SD), as well as the factor of improvement over unassisted coughing.

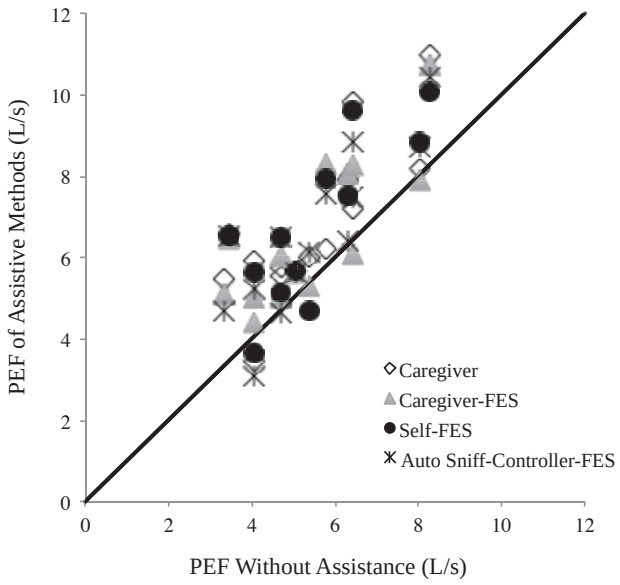

Fig. 5. Assisted coughing improves cough. All methods compared along the unit slope-line. Each dot is a subject at a method as indicated by the color and style legend. All assisted methods were better than unassisted (all dots above the line), and there was no difference between assistive methods.

IV. CONCLUSION/DISCUSSION

Experiments in 16 able-bodied participants allowed us to identify the precise point of glottis closure using the sniff-controller, and experiments in 14 subjects with SCL verified that the sniff controller can effectively time and trigger FES-induced cough. A key novel feature of this study was the synchronized measurements of nasal airflow with endoscopic video of cough events. This contributed a compelling demonstration of the process of glottis closure and its relationship to nasal airflow and neck and abdominal muscle contraction. It was this combination that allowed us to identify the critical time-point and duration for FES activation. This also provided for several novel observations, such as the neck muscle contraction that started before the abdominal muscles contraction and glottis closure during cough. This may reflect an accessory muscle contribution to the inspirium that precedes cough.

All assistive methods tested in this study improved cough efficacy compared to unassisted cough by about 25%, and reached about 76% of the mean expected values of PEF based on European Respiratory Society standards of able-bodied people (8.78 ± 0.75 L/s) [38]. Here these values were obtained by delivering current through two large abdominal surface electrodes. This configuration of stimulation electrodes provides extensive coverage, and minimizes the need for accuracy in placement. That said, this study was aimed at examining sniff-controlled triggering of FES and not electrode design and placement. Thus, we varied method of triggering across conditions but kept the electrodes constant. It is conceivable that the large electrodes we used were perhaps less advantageous or convenient for some participants. Moreover, we did not titrate or systematically test the influence of the altered current density likely associated with this electrode configuration. Thus, we cannot make any statements as to any advantages or disadvantages associated with this electrode design. The issue of electrode design and placement should be further studied separately [39], and here we can make conclusions solely regarding methods of triggering. Indeed, given the current results with surface electrodes, we speculate that the sniff-controller can be equally used to accurately time and trigger other methods for stimulation and cough induction, such as spinal epidural electrodes [40], microstimulators [41] or magnetic stimulation of the thoracic nerve roots [42, 43].

There are several methods to self-trigger FES. Alternatives range from a simple button, to chin-joystick activation [19], and to EMG signals obtained from either the pectoralis major muscle or the deltoid muscle [20]. Furthermore, our approach is not the only one to trigger FES off the respiratory trace itself [23]. Initial efforts in this direction used the signal obtained from a full-mask spirometer [25], and it was hypothesized that modifications in the ensuing FES output would allow its application for chronic use [26]. Whereas a full-mask spirometer may be considered obtrusive, an important modification has been the extraction of the respiratory trace from plethysmographic belts and its application to FES triggering for both assisted ongoing

respiration and assisted cough [27, 28]. Each of these methods has its advantages and disadvantages. Triggering off plethysmographic belts is very attractive because these are the least obtrusive of the methods tested. The value of this advantage cannot be overstated. In turn, a direct comparison implies that plethysmographic belts provide a less sensitive measure of airflow events [44], and they cannot account for transient events of paradoxical breathing where the chest and abdomen reverse direction in relation to inhalation and exhalation, a common occurrence in able-bodied and paralyzed individuals alike [45, 46]. Indeed, given these issues, to the best of our knowledge FES triggering by plethysmographic belts has yet to be tested in SCL patients. The disadvantages of the sniff-controller presented in this study are first and foremost its esthetic quality. A nasal cannula has the "look of disease", and it will not be readily worn by users in public. This largely restricts its application to sessions dedicated to coughing in privacy, and limits/prevents its application as an assistive tool for ongoing respiration (except perhaps in a hospital rehabilitation setting). Moreover, the sniff-controller method will likely fail all together in cases of a completely stuffed nose. Given that a stuffed nose is more likely exactly at times where cough is more important, this is a meaningful weakness. Finally, for the sake of consistency with most other studies, here we applied FES in the supine position. Although several studies imply only minimal differences in FES outcome as a function of posture [39, 42], such differences may nevertheless materialize because abdominal muscle length is slightly increased supine compared with seated [47]. Thus, the influence of posture on sniff-triggered FES remains to be investigated. In turn, the advantages of the method presented in this study are its simplicity (hence potential low cost if commercialized), its robustness, and its temporal accuracy. Moreover, patients with all levels of paralysis can independently activate the system. This provides for a critical component of independence and freedom from caregiver. Finally, and critically, we demonstrated that it works in paralyzed individuals. Indeed, several subjects in this study noted the added privacy and independence that this system affords, and also spontaneously subjectively stated that using the sniff-controlled system they experienced the "best" cough they remember in years since injury. With this in mind, we conclude that future developments aimed at developing a smaller wireless nasal sensor to replace the nasal cannula may provide for an optimal sniff-controlled system that will be used by patients in need.

APPENDIX

The Sniff Controller-FES Device Code

```
// ==================== Define pins ====================
const int ledPin =  13;
const int analogInPin = A6;  // Analog input pin
const int startPin = 2;      // Red Button
const int pulsePin = 3;      // Output pin
const int manualPin = 4;     // Monitors manual pin status can be LOW or HIGH - Stimulation mode
const int sniffPin = 5;      // Standby mode activation - Sniff / Button mode

// ==================== Define pulse parameters ====================
const int pulseDelay = 50;    // in ms
const int pulseFreq = 100;      // in Hz
const int pulseDuration = 500;  // in ms

// ================Define Cough Detection Parameters ================
const int timer = 1;   // The time scale of the data from the sensor
const int duration = 40;   // Time window to detect the cought 40 points = 58-59 ms
const int length = duration / timer; //Time window translated to ms
const int length2 = 4; // inhale verification - short length to catch the spike
                       //(To know that you are below a minimum) - set to zero to cancel this test
const float meanx = ( (float(length) / 2) - 1 ) / 2; //constant number for the mean value of x, depends on legth
const float tb1 = -4;   // slope b threshold, for fast glottice closure

// ========================== Define vairiables ==========================
int memory[length]; //Will save last sensor data
int counter = 0; //Used to save last point that data was saved
float varx = 0;  //saves the variance of x
float meany1 = 0; //saves the mean y value in the last 40 ms
float meany2 = 0; //saves the mean y value in the last 4 ms
float b1 = -100; //saves current slope
float b1_old = -100; //save last slope

unsigned long ADCTimer = 0; //used to save current time
const int ADCDt = 20; // scan interval
int analogIn = 440; //saves last analog in for sniff detection
int analogInOld = 440; //saves last analog in for sniff detection
const int upperThreshold = 500; //upper threshold for sniff detection
int sniff = 0; //Detected sniff in the
int sniffOld = 0; //Was sniff detected last scan time (ADCDt)
unsigned long sniffTimer = 0; //used to store time from last sniff
const int tShort = 2000; // time interval two short sniffs should occur
int STATE = 1; // Saves the state of the systme State = 1 - manual, State = 21 - Sniff, State = 22 - Button
int coughDetection = 0; //should go to sniff Detection state
int coughTrigger = 0; //should trigger cough

// ================================================================

// Function to setup communication
// The function also sets up varx - variance of uniform variable (1, length)
void setup() {
  // initialize serial communications at 9600 bps:
  Serial.begin(9600);
  pinMode(pulsePin, OUTPUT);
  pinMode(ledPin, OUTPUT);
  pinMode(startPin, INPUT);
  pinMode(manualPin, INPUT);
  pinMode(sniffPin, INPUT);
  digitalWrite(pulsePin, LOW);
  digitalWrite(startPin, HIGH);
  digitalWrite(manualPin, HIGH);
  digitalWrite(sniffPin, HIGH);
  digitalWrite(ledPin, HIGH);

  for (float i = 0; i < (length / 2); i++) {
    varx += pow(i - meanx, 2);
  };
  varx = varx / (length / 2);
}

// Function that sets the state of the box in each iteration of the main loop of the controller
// State machine model
void setState(){
    if (digitalRead(manualPin) == LOW) {
        STATE = 1;
    }
    else { //(digitalRead(manualPin) == HIGH
        if (digitalRead(sniffPin) == LOW) {  //manual pin is off sniff pin is on
            STATE = 21;
        }
        if (digitalRead(sniffPin) == HIGH) { //manual pin is off sniff pin is off
            STATE = 22;
        }
    }
      Serial.println("");
      Serial.print(STATE);
      Serial.print(" ");
      Serial.print(coughDetection);

}

// A function to print out the log while monitoring the sniff device
// Prints out to screen the state of several varialbe
void printToLog() {
```

```
  for (int i = 0; i < length; i++) {
    Serial.print(memory[i]); //prints the readout of the device
    Serial.print(" ");
  }
  Serial.println("");
  for (int i = 0; i < (length/2); i++) {
    Serial.print(memory[(counter + 1 + i) % length]);
    Serial.print(" ");
  }
  Serial.println("");
  for (int i = 0; i < (length/2); i++) {
    Serial.print(memory[(counter + (length / 2) + 1 + i) %
length]);
    Serial.print(" ");
  }
  Serial.println("");
  Serial.print(counter);
  Serial.print(" ");
  Serial.print(meanx);
  Serial.print(" ");
  Serial.print(varx);
  Serial.println("");
  Serial.print(meany1);
  Serial.print(" ");
  Serial.print(meany2);
  Serial.print(" ");
  Serial.print(b1);
  Serial.print(" ");
  Serial.println(b1_old);
}

// ======================== Main loop of the controller
=======================
void loop() {
  while (1) { //main loop
    setState(); //sets the state of current iteration according to
the pin states

    // This part is used for the simple function - on mode -
red button function
    if (STATE == 1) { //Manual mode
      // In initial stage, when manual pin is off only monitors
start pin and manual pin
      while ((digitalRead(startPin) ==
HIGH)&(digitalRead(manualPin) == LOW)) { //Check red
button triggering or mode was changed
      }
      if (digitalRead(startPin) == LOW) { //Validate that red
button was pressed
        coughTrigger = 1; //Cough was triggered by red button
      }
    }
    else if (STATE == 21) { //Monitor double sniff
      while ((coughDetection == 0)&(digitalRead(sniffPin)
== LOW) & (digitalRead(manualPin) == HIGH)) { //checks
that state did not change
        if ( (millis() - ADCTimer) > ADCDt )  { //checks
that scan interval did not change
          ADCTimer = millis(); //save current time
          analogInOld = analogIn; //stores previous read of
the signal
          analogIn = analogRead(analogInPin); //read new
signal
          Serial.println(analogIn);

          if ( (analogIn > upperThreshold)&(analogInOld <
upperThreshold) ){ //did the signal cross the threshold?
            sniff = 1; //sniff was detected
          }
          else {
            sniff = 0; //sniff was not detected
          }

          if (sniff != 0) { //look for the second sniff
            if ( ( (millis() - sniffTimer) > tShort)&(sniffOld
!= 0) ) {//clears first sniff detection
              sniffOld = 0;
            }
            if (sniffOld > 0) { //cough detection standby -
the system is ready for cough detection
              coughDetection = 1;
              sniff = 0;
              sniffOld = 0;
              Serial.println("Detect in 21");
            }
            else { //first sniff detection sets up the timer
              sniffTimer = millis();
              sniffOld = sniff;
            }
          }
        }
      }
    }
    else if (STATE == 22) { //Wait for red button press
      // PB detection
      while ((digitalRead(startPin) == HIGH)
&(digitalRead(sniffPin) == HIGH) & (digitalRead(manualPin)
== HIGH)) {
        }
        if ((digitalRead(sniffPin) == HIGH) &
(digitalRead(manualPin) == HIGH)) {
          delay(10);
          coughDetection = 1;
          Serial.println("Detect in 22");
        }
    }
    if (coughDetection == 1) { // Go to cough detection
      delay(1000);
      // reset analog read memory - for computing sniff
threshold
      for (int i = 1; i < length; i++) {
        memory[i] = 0;
      }
      counter = 0;
      digitalWrite(ledPin, LOW); //change led state

      while (coughDetection == 1 & digitalRead(manualPin)
== HIGH){ //cough detection loop
        memory[counter] = analogRead(analogInPin);
```

```
            meany1 = 0;
            meany2 = 0;

            b1_old = b1; // fixed for this run
            b1 = 0;

            for (int i = 0; i < (length / 2); i++) {
               meany1 += memory[(counter + 1 + i) % length];
               if (i < length2) {
                 meany2 += memory[(counter + (length / 2) + 1
+ i) % length];
               };
               b1 += float(i) * memory[(counter + 1 + i) %
length]; // Start point is in memory
            };

            meany1 = meany1 / (length / 2);
            meany2 = meany2 / (length2); // changed to length2
            b1 = (b1 / (length / 2) - meanx * meany1) / varx;

            if ( (b1 < tb1) & (meany1 > 450) & (meany2 < 450)
) {
               delay(pulseDelay);
               coughTrigger = 1;
               coughDetection = 0;
               Serial.println(b1_old);
            }
            counter = (counter + 1) % length;
            //printToLog();
            delay(timer); // Sleep between operations
         }
      }
      if (coughTrigger == 1) { //cough was triggered, do the
output squence
         tone(pulsePin, pulseFreq, pulseDuration);
         digitalWrite(ledPin, HIGH);
         delay(pulseDuration);
         coughTrigger = 0; //set back the variable
      }
   }
}
```

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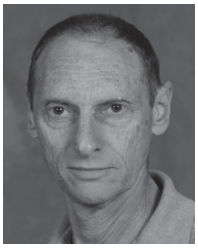

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