Relationship between resistive loads and P1 peak of respiratory-related evoked potential

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Knafelc, Marie, and Paul W. Davenport. Relationship between resistive loads and P1 peak of respiratory-related evoked potential. J. Appl. Physiol. 83(3): 918–926, 1997.—This study investigated the relationship between resistive-load (ΔR) magnitude, the first positive peak (P1) amplitude of the respiratory-related evoked potential (RREP), and load-magnitude estimation (ME). The first experiments determined the subject’s (n = 9) ME of five ΔR magnitudes randomly presented at the onset of an inspiration or by interrupting an inspiration. No significant differences were found in the slopes of the two different presentations, but the subjects estimated the interrupted inspiratory loads to be of lesser magnitude than loads presented at the onset of the breath. In the second series of experiments, the subject’s (n = 6) RREPs were recorded in response to three ΔR magnitudes. The amplitude of the short-latency P1 peak of the RREP significantly increased with increases in the ΔR magnitude. A log-log plot of the group-averaged P1 amplitudes showed a linear relationship with ΔR. These results were consistent with the hypothesis that the perceptual magnitude of the respiratory load was related to the P1 amplitude of the RREP, suggesting the physical magnitude of the load-related stimulus was correlated with the amplitude of the cortical neural activation.

first positive peak; cortical-evoked potentials; magnitude estimation; respiratory sensation; inspiration

THE DETECTION of added inspiratory loads to breathing, usually resistive or elastic, has been studied by using difference threshold methods (3, 8). The load-detection threshold has been shown to be a constant fraction of the background load intrinsic to the respiratory apparatus and the subject (26). Magnitude estimation (ME) of inspiratory loads has been studied by using scaling methods (2, 6, 25). The studies have shown that the perceived magnitude of an increased extrinsic load is linearly related to the load magnitude when a log-log transformation is used (6, 18, 25). It has also been demonstrated that human subjects can easily scale a variety of respiratory parameters other than mechanical loads, i.e., volume, pressure, ventilation, and frequency (2, 6, 15, 18, 25). Psychophysical studies have thus shown that human subjects can detect the presence and type of extrinsic load and assign a perceptual scale to respiratory stimuli associated with the mechanics of ventilation. The results, however, provide little information on the afferent transduction and neural processing mechanisms mediating load sensation.

The activation of cortical neurons by mechanical loads has been studied by using evoked-potential techniques to investigate the neural mechanisms mediating respiratory-load sensation. A mechanical load (inspiratory occlusion) was applied while simultaneously recording from the somatosensory region of the cortex in the adult human (10, 19). These investigators reported inspiratory occlusion-elicited respiratory-related evoked potential (RREP) recorded in the somatosensory region of the cortex. The evoked potential was similar to mechanically elicited somatosensory-evoked potentials (SEP) reported for the hand and leg. The first peak observed in all subjects, P1, was a positive voltage that was suggested to be an exogenous peak because of the dipole that occurs when a cerebral cortical column is depolarized by the arrival of activity from a population of afferents that are activated by the occlusion stimulus. It has also been demonstrated that this RREP can be elicited by occlusions presented either at the onset of inspiration or by interruption of the breath after the onset of the inspiratory effort (near midinspiration) and is present bilaterally in the somatosensory region (19). However, inspiratory occlusions were the only mechanical load tested, and the relationship of the RREP to the perception of a ventilatory load has not been determined.

Franzén and Offenloch (14) reported that the magnitude of the early positive peak of the touch (finger)-elicited SEP (analogous to the RREP P1) was correlated with mechanical stimulus amplitude and ME of the touch. It was reasoned that, if the RREP is a SEP, then the amplitude of the P1 peak of the RREP should correlate with the load magnitude and associated ME. The purpose of the present investigation was to test the hypothesis that the stimulus magnitude [resistive load (ΔR) magnitude] and the P1 amplitude of the RREP are directly correlated. The method for eliciting the RREP was interruption of inspiration.

METHODS

Study 1: ME of ΔR

The first study was performed to determine whether a subject’s ME of ΔR presented as an interruption of inspiration was similar to ME of these loads presented at the onset of inspiration.

Subjects. Five men and four women (average age = 26 yr) with no history of pulmonary or neurological disease participated in the first protocol. The Institutional Review Board, J. Hillis Miller Health Center, University of Florida, reviewed and approved both protocols used in this project. All subjects were informed of the nature of the study before starting the experiment, and written consent was obtained.

Procedure. The subject was seated comfortably, semireclined in a lounge chair. The subject wore a noseclip and respired through a mouthpiece (Fig. 1) and nonrebreathing valve (2600 series, Hans Rudolph). Care was taken to suspend the valve to eliminate the need for the subject to bite the mouthpiece while maintaining an airtight seal. The ΔR were sintered bronze disks placed in series in a Plexiglas tube (loading manifold), with stoppered ports between the disks...
Mouth pressure (Pm) was recorded from a port in the center tubing to the inspiratory port of the nonrebreathing valve. (Fig. 1). The loading manifold was connected by reinforced tubing to the inspiratory part of the nonrebreathing valve. The loading manifold was hidden from the subject’s view. Mouth pressure (Pm) was recorded from a port in the center of the valve. Pm was sensed with a differential pressure transducer and signal conditioner (model 12, Grass Instruments). Pm was displayed on an oscilloscope and used for timing the load application.

Five magnitudes of inspiratory resistance (2, 5, 9, 13, and 21 cmH2O·l−1·s) were presented at the onset of an inspiration and after the onset of the breath as an interruption of an inspiration. The onset-load trials were presented for the entire inspiratory effort by manually inflating a balloon (Hans Rudolf) that closed the balloon occluder (Rmin) port of the loading manifold (Fig. 1) during inspiration and channeled the airflow for the subsequent inspiration through the selected R port. The interrupted-load trials were presented for ~500 ms with the same loading manifold by manually inflating the occlusion balloon after the inspiration had started, using the onset of negative Pm to indicate the beginning of inspiration. All five load magnitudes were presented a total of 10 times each for both onset and interrupted inspirations. The ME of each load trial was obtained by using a handheld meter with a modified Borg scale (4). Subjects used the single turn knob to position a needle on a meter that corresponded to the subjective rating of the magnitude of the resistance. The scale was anchored at both ends by allowing the subject to experience no resistance (0%) and complete resistance. The scale was anchored at both ends by allowing for an uninterrupted inspiration. The balloon occluder was connected to the opening of this port. The inspiratory load was presented as described above for an interrupted inspiration. The balloon pressure was used to trigger the computer for data sample collection. Each load was separated by two to six unloaded breaths. The load was applied for a duration of ~500 ms. Three ΔR from the first study were used that exceeded the detection threshold (ΔR1 = 2.0, ΔR2 = 9.0, and ΔR3 = 21.0 cmH2O·l−1·s). Inflation of the balloon with the no-load (R0) port open served as the control for acoustic or other artifacts associated with the load application.

For each subject, ordering of the four respiratory load levels was arranged to minimize temporal, order, and sequence effects in the following manner. Subjects received four sets of 80 trials each, with a rest period taken between each of the sets. Within each set of 80, load trials were tested by using 16 blocks of five trials each, with the same load presented within a block to minimize manifold manipulations. Ordering of the different blocks was randomly determined, with the restriction that each successive set of four blocks contained only one block of each load level. Thus, over the set of 80 trials, each block of five trials of a given load was presented four times (20 total trials). The randomization was independently drawn for each set of 80 trials and for each subject. There were four experiments, making 80 trials of each load magnitude available for signal averaging. Each experiment was separated by a rest period. The requirement to present
all four sets was ~2 h. Including subject preparation time, the entire study session lasted <3 h.

Data Analysis

For each load presentation, 500 ms of EEG activity, Pm, and balloon pressure were digitized at 3 kHz and stored on disk for subsequent computer-signal averaging (SIGAVG, Cambridge Electronic Design). Although the digitizing frequency was greater than the high-frequency filter (1 kHz), which could lead to aliasing, the frequency at maximum power of the RREP $P_1$ peak was $\times 30$ less than the high-filter frequency and $\times 100$ less than the digitizing frequency, which would make aliasing of the $P_1$ minor or nonexistent. Each load magnitude was averaged separately. The computer stored the individual load trials in the order of presentation. The signal-averaging program recalled from memory the first stored the individual load trials in the order of presentation. Load magnitude was averaged separately. The computer averaged EEG traces. The $P_1$ peak is the first initially positive peak amplitude was then measured in microvolts from the control-subtracted averaged traces. The $P_1$ peak amplitude and latency were measured. The $P_1$ peak amplitude was then measured in microvolts from the control-subtracted averaged traces. The $P_1$ peak amplitude was correlated with the resistive-load magnitude by using a log-log transformation.

The ME, with loads presented by interruption of inspiraion from the first experiment for the $\Delta R$s used in the RREP experiment for each subject, were correlated with the $P_1$ amplitude for that load using a log-log transformation. In one subject, a ME of the fifth load application in each load block was obtained during the RREP trial. A light was turned on to cue the subject to provide an estimate of the load on the next inspiration. Subjective rating of the perceived intensity of the $\Delta R$ was provided using a modified Borg scale, as described in study 1.

A two-way analysis of variance (ANOVA) was used to test for differences between treatments, and one-way ANOVA was used for comparisons within individuals between the reported ME and $\Delta R$, and between the $P_1$ peak amplitude and peak latencies of the RREP. These results were also subject to a one-way repeated-measures ANOVA for multiple factors. A linear regression of the log-log plot was also performed. The level of significance was set at $P < 0.05$.

Study 3: Noncefhalic RREP Source Controls

To determine whether there was a change in head motion during the application of the $\Delta R$, a series of control experiments was performed on eight subjects (2 females, 6 males, age 11–24 yr) with no history of pulmonary or neurological disease. The subjects were prepared as previously described for recording EEG activity. The subject was again seated in the same semireclined position in the chair with an air-filled pillow positioned under his or her head. The subject’s head was centered on the pillow by using the inion as the head reference point. The pressure in the pillow was recorded with a pressure transducer connected to a differential pressure transducer. Motion of the head was recorded by a change in the pillow pressure. A 1 cm H2O change in the pillow pressure corresponds to a 7.5-mm displacement between the head of the subject and the chair headrest. The subject responded to a nonrebreathing valve, as described previously. The RREP $\Delta R$ protocol was repeated by using three magnitudes of $\Delta R$ ($\Delta R_1 = 4.0, \Delta R_2 = 12.0$, and $\Delta R_3 = 22.6$ cm H2O l $-1$ s). The EEG activity, motion pressure, and Pm were digitized at 2 kHz and stored on computer disk. EEG activity from Cz–C3 and Cz–C4 and the two pressure signals were averaged as described for the $\Delta R$ RREP protocol.

Another series of experiments was performed on five subjects (males, age 21–27 yr) to record the activity from the cephalic electrodes and electrodes placed over the dorsal surface of the neck and thoracic spine. The subjects were presented as described for the $\Delta R$ RREP experiments. Scalp electrodes were placed at C3, Cz, and C4. In addition, surface cup electrodes were placed at the cervical spinal C1 (spC1) and C7 (spC7) sites and at the thoracic spinal T12 (spT12) site. The electrode pairs recorded were C2–C3, C2–C4, spC1–spC2, spC7–spC7, and spC7–spT12. These signals were amplified and band-pass filtered (1 Hz–1 kHz). The subject respired through the nonrebreathing valve with Pm recorded at the center of the valve. One magnitude of $\Delta R$ (17.6 cm H2O l $-1$ s) and no load were presented as interruptions of inspiration. Two trials, each with 100 load presentations, were performed with a rest period off the apparatus separating the trials. Each load presentation was separated by two to five unloaded breaths. Each load trial was separated from the load trial by using a no-load control trial. The electrooculogram (EOG) was recorded with surface cup electrodes placed on the lateral edge of the left eye. EOG activity was observed throughout the recording session, and a load presentation was rejected from the trial if eye-blink-related EOG activity was present.

The Pm, cephalic, and spinal signals were averaged for the load and no-load trials. For the two load trials, the signals from both trials were initially averaged (a total of 200 presentations available for averaging) without exclusion of electrocardiogram (ECG) artifacts and then reaveraged with ECG artifacts excluded. The three signals were displayed and examined for the presence of ECG activity characterized by large qrs-wave-associated voltage changes in spC1–spC2, spC7–spC7, and spC7–spT12 signals for each individual presentation. For the averages with ECG excluded, the presentation was included in the average only if the initial 300 ms of the poststimulus epoch was free of large qrs-wave-associated voltage changes.

RESULTS

Progressive increases in the magnitude of $\Delta R$ presented at the onset of the breath were linearly related on a log-log scale ($R^2 = 0.94$) to an increase in the estimated magnitude of the load by the subject (Fig. 2). The slope of the line was 0.72. When the same resistances were presented as an interruption of the inspiration, there was again a linear log-log relationship ($R^2 = 0.98$) between the $\Delta R$ magnitude and the subjects’ estimation of the load (Fig. 2). The slope was 0.70 and not significantly different from when the loads were presented at the onset of the breath. However, the
subjects estimated the magnitude of the midinspiratory loads as smaller than for onset presentations (Fig. 2).

The RREP P1 peak amplitudes increased with the increase in the inspiratory \( \Delta R \) magnitude (Fig. 3). The P1 peak amplitudes and their latencies are summarized in Table 1. There were no significant differences in the peak latencies for all load magnitudes. The increase in RREP P1 peak amplitudes was observed in both electrode pairs, C2–C3 and C2–C4. There was a linear log-log relationship \( (R^2 = 0.99) \) between the P1 amplitudes and the \( \Delta R \) magnitude (Fig. 4). The slope of both lines was 0.35, and there were no significant differences between CZ–C3 and CZ–C4 electrode pairs.

The \( \Delta R \) magnitude had a linear log-log relationship with the ME of the resistive loads and the RREP P1 amplitudes. When the results for the two studies were combined, there was also a log-log relationship \( (R^2 = 0.996) \) between ME and the RREP P1 amplitudes of the same loads (Fig. 5). The slopes were 2.20 and 2.68 for C2–C3 and C2–C4, respectively, and were not significantly different. For the one subject in whom this comparison could be made, the relationship between P1 peak amplitude and ME determined in study 2 was the same as the P1 peak amplitude-ME relationship using the ME results of study 1.

In study 3, there was a small, normal breathing-related movement of the head, as evidenced by a motion-pressure increase and decrease in synchrony with inspiration and expiration, respectively. When an inspiratory load was applied, there was no change in the motion pressure observed in the individual load presentations (Fig. 6A). There was also no change in the averaged motion pressure for all load magnitudes (Fig. 6B).

The P1 peak of the RREP was observed in the averaged CZ–C3 and CZ–C4 signals for the \( \Delta R \) (Fig. 7), with no coincident peak found in the spC1–C2, spC1–spC7, and spC7–spT12 signals averaged with ECG artifact excluded (Fig. 7). The averages obtained without exclusion of ECG artifact did not alter the P1 peak in the C2–C3 and C2–C4 RREP waveforms (Fig. 8). However, the inclusion of ECG artifact in the averages for the other electrode pairs (spC1–C2, spC1–spC7, and spC7–spT12) produced voltage peaks that were not consistent among subjects.

**DISCUSSION**

The results of this study demonstrate that subjects can provide a ME of \( \Delta R \) presented at the onset of the inspiration or by interrupting inspiration. There is also

<table>
<thead>
<tr>
<th>Resistance, cmH2O·l·s</th>
<th>Amplitude, µV</th>
<th>Latency, ms</th>
<th>Amplitude, µV</th>
<th>Latency, ms</th>
</tr>
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<tbody>
<tr>
<td>2</td>
<td>1.58 ± 0.58</td>
<td>52.2 ± 3.7</td>
<td>1.36 ± 0.27</td>
<td>51.1 ± 1.7</td>
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<tr>
<td>9</td>
<td>2.51 ± 0.50</td>
<td>49.7 ± 2.3</td>
<td>2.43 ± 0.58</td>
<td>47.8 ± 1.9</td>
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<tr>
<td>21</td>
<td>3.66 ± 0.67</td>
<td>56.3 ± 2.4</td>
<td>3.09 ± 0.46</td>
<td>56.2 ± 1.3</td>
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Values are means ± SE. P1, first positive peak; RREP, respiratory-related evoked potential; C2, C3, and C4, scalp positions for EEG.
a direct correlation between the amplitude of the P1 peak of the RREP and the magnitude of the ΔR. In addition, the P1 peak of the RREP recorded with CZ–C3 and CZ–C4 electrode pairs is not an artifact of head motion, neck and thoracic muscle activity, or ECG activity.

ME of ΔR requires the subjects to provide an estimate of the sensory magnitude of a suprathreshold load by using a numerical scale or by cross-modality matching, i.e., the magnitude of handgrip force matched to the perceived magnitude of the load (6, 25). Respiratory mechanical load sensation follows the general psychophysical relationship (Steven's Psychophysical Law), i.e., the magnitude of the sensation and the stimulus intensity is a power function related to the stimulus conditions and type of stimulus. The results of the present study, using load presentations at the onset of the inspiration, are consistent with these previous reports for ΔR ME. ME of ΔR presented as interruptions of the inspiration resulted in a similar slope, indicating that the sensitivity of the subject to the ΔR is unaltered by the timing of the load presentation. However, the interrupted loads were estimated to be of smaller magnitude than the same loads presented at the onset of the breath. It has been shown that with increased inspiratory durations, the ME of ΔR increased (18). The interrupted application of ΔR used in the present study resulted in a reduced duration of inspiration against the load. The reduction in the ME of interrupted load presentations due to a shorter duration of inspiration against the load would be predicted from the report of Killian et al. (18). The similarity in slope, however, suggests that the sensitivity of the subject to the load is less dependent on the duration of the stimulus. Although the ME of ΔR using interrupted inspiratory presentations were perceived with the same sensitivity as the onset presentations, the systematic decrease in the perceived magnitude of the loads supports the notion that the duration of the inspiration against the load affects the perceived magnitude of the load (18). These results, however, provide little information on the afferent transduction and neural processing mechanisms mediating load sensation; yet, to correlate the ME relationship with the P1 peak amplitude of the RREP elicited by inspiratory interruption, it was necessary to determine the ME relationship for interrupted load presentations.

The activation of cortical neurons by mechanical loads has been studied using evoked-potential techniques similar to those routinely used in other somatosensory systems (1, 5, 14, 20, 27). Inspiratory occlusion was applied at the onset of inspiration, while simultaneously recording from the somatosensory region of the cortex in the adult human (10). Signal averaging began from the onset of inspiration. This analysis resulted in the observation of occlusion-elicited evoked potentials, RREP, recorded in the left somatosensory region of the cortex. Four voltage peaks were reported in all subjects. The P1 peak was a positive voltage that was suggested to be due to the dipole that occurs when a cerebral cortical column was depolarized by the arrival of activity from a population of afferents that were activated by the occlusion stimulus. Revelette and Davenport (19) demonstrated that the RREP can be elicited by occlusions presented either at the onset of inspiration or

![Fig. 4. Log-log relationship between amplitude of P1 and ΔR magnitude.](image1)

![Fig. 5. Log-log relationship between amplitude of P1 and magnitude estimation of ΔR.](image2)
with interrupted inspiration. The RREP was present bilaterally (19). The evoked potential elicited by interruption of inspiration had a shorter latency for the P1 peak, which was probably due to the more rapid onset of the stimulus.

In the present study, the methods used for presentation of the load for eliciting the RREP were identical to previous reports from this laboratory (11, 19). The various magnitudes of the loads were presented in a randomized block design to control for variations in ventilatory pattern that normally occur in subjects that might affect the RREP. The number of presentations for each load magnitude were equal for each set of trials, including the control no-load presentation that allowed for the resultant averaged signals to reflect the response to the load throughout the entire experiment. The number of load presentations available for averaging is greater than the 32 reported as a minimum for observing the RREP (19) but less than the number of stimuli commonly presented for other somatosensory systems (1, 5, 14, 20, 27).

The restriction in the number of presentations available for averaging is due to the unique constraint for recording respiratory-evoked potentials of being able to present only one load per breath and the necessity to have unloaded control breaths between loaded breaths. The upper limit for load presentation number is the amount of time a subject can tolerate respiring on the loading apparatus. In this study, each load magnitude was presented 80 times. This was found to be an acceptable compromise for reliably observing the P1 peak of the RREP, accommodating subject tolerance of the protocol, and maximizing the number of presentations for averaging. The use of the point of intersection of two tangent lines on the Pm tracing for determining the time 0 point for measurement of peak latencies (11) has allowed for a standard and consistent zero point for all subjects. The application of the load occurred with the inflation of a balloon in the breathing circuit. This balloon inflated silently; however, the subtraction of the control no-load average from the loaded average removes residual non-load-related artifacts (such as

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**Fig. 6. Effect of interruption of inspiration with a resistive load on motion of head.**

A: application of R3 load (22.6 cmH2O·L⁻¹·s⁻¹) as an interruption of inspiration. Top: pressure in air-filled pillow used to record motion of head. Change in motion pressure of 1 cmH2O corresponds to 2.75-mm motion. Bottom: Pm. Vertical line, onset of load that produced increased negative Pm and no change in motion pressure. These traces are for single load presentation in individual subject. B: averaged response to application of R3 (22.6 cmH2O·L⁻¹·s⁻¹) loads as interruption of inspiration for individual subject. A total of 92 R3 presentations were averaged for this subject (same as in A). Top: averaged Cz–C3 activity, with P1 indicated; middle: averaged motion pressure; bottom: averaged Pm. There was no change in averaged motion pressure with R3 loads. Identical motion pressure responses were obtained for the R1 and R2 loads (4.0 and 12.0 cmH2O·L⁻¹·s⁻¹, respectively; not shown).
auditory and vibration effects) from the load-elicited RREP. The methods used in this study controlled for variability in ventilatory pattern, allowed for consistent measurement of latencies, maximized the number of load presentations, and minimized potential artifacts.

It is possible, however, that the recordings of the peaks of the RREP, including P1 under investigation, were contaminated by other non-stimulus-related artifacts. The control, no-load averages obtained during all trials showed no peaks coincident with the P1 peak. The fact that the P1 peak was unaltered when the control, no-load average was subtracted for each load's averaged RREP demonstrated that the P1 peak observed with ΔR was not contaminated by sound or apparatus-related artifacts. The subjects in this study were in a semireclined position, with the back, neck, and head fully supported. When head motion was recorded as a change in the pressure of an air-filled pillow, there were ventilation-related slow changes in head motion that were synchronized to inspiration and expiration. The application of a ΔR by inspiratory interruption produces a sudden impediment in the normal thoracic pattern of expansion. However, there was no additional change in head motion observed for all load magnitudes. The absence of load-related changes in head motion, which could cause movement of the scalp electrodes, means that such a motion artifact did not contaminate the RREP.

Sudden interruption of inspiration by occlusion has been shown to produce a short-latency, transient inhibition followed by a brief facilitation of neck and intercostal muscle electromyogram (EMG) activity (7). Interruption of inspiration with ΔR could produce a similar voltage change in the neck and intercostal muscle EMG, and these voltage changes possibly alter the P1 peak of

Fig. 7. Averaged response to inspiratory ΔR (17.6 cmH2O·l·s) recorded in cephalic and spinal EEG electrodes, with ECG artifacts excluded. A total of 70 load presentations were averaged. Top 2 traces: C3 and C4 referenced to vertex Cz. Third trace vertex referenced to electrode placed at C1 cervical spinal position (spC1). Fourth trace: electrode placed over cervical spinal C2 position (spC2) referenced to spC1. Fifth trace: electrode placed over thoracic spinal T12 position (spT12) referenced to spC7. Electrooculogram (EOG) is averaged response recorded with bipolar electrodes placed on lateral border of left eye. Bottom: averaged Pm.

Fig. 8. Cephalic referenced RREP elicited with resistive load. ECG was observed from spinal electrode pairs: spC7 referenced to spC1 and spT12 referenced to spC1. P1 is indicated. RREP was averaged when qrs artifact of ECG was absent (A) and when qrs artifact of ECG was present (B) in spinal electrodes. A: averaged response recorded in C2–C3 and C2–C4 with ECG artifacts excluded. A total of 70 load presentations free of ECG artifacts in spinal signals was averaged. These traces are same as in Fig. 7. B: averaged response recorded in C2–C3 and C2–C4 with ECG artifacts included. A total of 170 load presentations was averaged.
the RREP. The simultaneous recording from sites on
the surface of the back in the region of the neck and
thorax did not directly record the EMG signal from
neck and intercostal muscles. However, EMG activity
changes in these muscles elicited by interruption of
inspiration with ΔR would generate voltage shifts in
the averaged response if such activity were evoked by
the load. No peak coincident with the RREP P1 peak in
C2–C3 and C2–C4 was observed in the neck and thoracic
electrode pairs. A reduction in EMG activity during the
P1 latency window should, in fact, favor the observation
of load-related activity in the EEG recordings.

In addition, the close electrode spacing of the C2–C3
and C2–C4 electrode pairs makes the recording of distant,
noncerebral voltage changes less likely. This is further
supported by the absence of ECG-related changes in the
C2–C3 and C2–C4 signals. The large amplitude
components of ECG activity produced peaks in the
spinal electrodes (spC1–spC7 and spC7–spT12). These
peaks were absent when the signals were averaged
when the load stimulus occurred during the t–p inter-
val of the ECG. The averages, obtained with these large
electrical-voltage changes associated with the ECG excluded, showed
no peaks in spC1–spC7 and spC7–spT12, demonstrating the absence of
ΔR-related changes in bioelectrical activity from these regions recordable by these methods.

This means that the P1 peak of the RREP recorded from
the C2–C3 and C2–C4 electrode pairs is not contami-
nated with ECG activity or neck and thoracic muscle
EMG activity. Thus these results suggest that the P1
peak of the RREP recorded from C2–C3 and C2–C4 was
of cephalic origin and not contaminated by sound,
apparatus, motion, ECG, or neck and thoracic muscle
EMG artifacts when the recordings were made with the
back, neck and head, supported.

The RREP was elicited in the present study by
inspiratory interruptions and was present in all sub-
jects tested. The P1 peak was present for all ΔR
magnitudes. The latency of the P1 peak was unchanged
for all the loads. This is probably due to the use of
interruptions of inspiration as the method for applica-
tion of the loads. The rate of the onset of the stimulus
varies slightly with this method, whereas the primary
change is the magnitude of the ΔR. The relationship
between evoked-potential amplitude and the stimulus
magnitude was studied by Franze¨n and Offelench (14).
They demonstrated that the magnitude of the touch
(finger)-elicited SEP was correlated with the amplitude
of the mechanical-touch stimulus and the ME of the
stimulus, i.e., increasing magnitude of touch stimulus
resulted in an increase in the amplitude of the early
positive peak of the evoked potential. Zhu and Starr
(27) recorded the SEP in response to magnetic stimula-
tion of the gastrocnemius muscle. This stimulation
activated primarily Ia afferents by mechanical contrac-
tion of the muscle. They reported a graded increase in
the SEP early positive peak (P1,0) amplitude, with
increases in stimulus strength magnitude that were
directly related to the muscle mechanoreceptor activa-
tion. The early positive peaks from these studies (14,
27) are similar to the P1 peak of the RREP. Increasing

touch magnitude also produces an increase in single-
unit afferent activity (17, 23). The magnitude of air-puff
stimulation of the glabrous skin of the hand has been
reported to be directly related to the ME of the stimulus
magnitude (16). In that study, the authors recorded the
afferent multiunit activity in their human subjects. The
intensity of the stimulus was directly related to the
duration of the afferent activity, the number of impulses,
and (with a reduced slope) the frequency of discharge of the afferents. This demonstrates that the
ME of a tactile stimulus is related to the spatial and
temporal summation of the afferent activity elicited by
the stimulation. Strobel and Daubenspeck (21) re-
ported a similar increase in the early positive peak of
the evoked potential elicited with increases in negative
Pm stimulation. In the present study, the amplitude of
the P1 peak of the RREP correlated with the ΔR
magnitude. In addition, the magnitude of the ΔR
related with the ME of the load. If this peak is
similar to the early positive peak of the SEP recorded
with touch stimulation, then the amplitude of the P1
peak is a result of the spatial and temporal summation
of afferent activity elicited by inspiring against a ΔR.
These results suggest that this peak is a neural marker
of the afferent activation of the cortical region from
which the electrodes are recording. It is, therefore, not
surprising that ME increases with increasing P1 ampi-
tude because this neural measure reflects the magni-
itude of the ΔR to the subject is estimating.

Animal studies of the neural mechanisms mediating
respiratory sensations are limited. Dogs with a tra-
cheal stoma were behaviorally conditioned to signal the
detection of an inspiratory ΔR and occlusions (9). The
ΔR detection threshold and Weber fraction were found
to be similar to those in humans. The application of the
loads through the tracheal stoma of the dogs excluded
afferent systems in the mouth, nose, pharynx, larynx,
and upper trachea from mediating this sensation. The
remaining afferents would be lung, vagal, and respira-
tory muscle mechanoreceptors. The breathing pattern,
as measured by tidal volume, inspiratory duration,
expiratory duration, breathing frequency, minute venti-
lation, and expired Pco2, was not altered by near-
threshold, detected loads. This would make it unlikely
that vagal afferents or chemoreceptors were mediating
this load detection. Phrenic and intercostal muscle
afferents have been demonstrated to activate neurons in the somatosensory region of the cat cerebral cortex
(12, 13). Specific mechanical stimulation of intercostal
mechanoreceptors elicits a short-latency activation of
cat somatosensory cortical neurons (12). These animal
studies have demonstrated that the neural substrate
exists in the respiratory pump muscles for the hypoth-
osed respiratory muscle afferent mediation of me-
chanical load sensation. The afferent pathways, corti-
sal distribution, and neural mechanisms for respiratory
sensation in normal humans, however, remain specula-
tive.

In summary, the results of this study have demon-
strated that the amplitude of the P1 peak of the RREP is
directly related to the magnitude of the stimulus and
the subject’s estimation of that magnitude. The afferents and neural pathways mediating the RREP are unknown. Respiratory muscle afferents have transduction properties and cortical projection pathways consistent with their hypothesized role in respiratory-load sensation. If this respiratory-related cortical activity is similar to evoked potentials for other sensory systems, then the early P1 potential would represent the arrival of the sensory signal in the somatosensory region of the cerebral cortex, similar to the primary evoked potential found with cortical surface recordings in the cat (12, 13). The correlation of the RREP (as a reflection of cerebral cortical activity) with the magnitude of the respiratory load and perceptual magnitude suggests that conscious humans use cerebral cortical sensory and motor systems as one response mechanism to respiratory loads.

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