Neuroanatomic Correlates Involved in Respiratory Control: Application of a Simplified Breath Control Design With Functional MRI

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PURPOSE

To propose a simple controlled breathing model utilized with functional MRI (fMRI) to delineate the neuroanatomic correlates involved in respiration.

INTRODUCTION

Brain imaging offers a promising means of non-invasively mapping the neural centers regulating respiration. PET imaging and fMRI have delineated many of the regions of activation involved with volitional breathing [1,2], with fMRI providing higher temporal and spatial resolution of the two modalities [2]. Visualization of brain activation areas depends on hemodynamic changes, which result from focal neurologic activity following breathing pattern changes. Previously utilized methods of controlled breathing include mechanical ventilation [2] and hyperpnea [3], both of which require monitoring devices and airway circuitry equipment to maintain various physiologic parameters such as tidal volume and end-tidal CO2 levels. One function of such equipment is to control for large changes in blood CO2 levels, which might cause global hemodynamic changes independent of neural activation [4]. Although necessary in these previous studies, the need for mechanical devices might be obviated in the setting of a more simplified breathing paradigm, which in itself might control for confounding physiologic factors. We propose such an experimental model used with fMRI to demonstrate activation areas involved in respiratory control without the use of ventilation devices.

MATERIALS AND METHODS

All subjects were scanned on a 3T GE MR magnet using a single-shot gradient-echo EPI sequence (TR 2.5 sec/TE 35 msec; FOV 24 cm x 24 cm; matrix size 64 x 64; slice thickness: 5mm (skip 1) echo spacing time 0.592 msec) sensitive to BOLD signal. Subjects were trained in the method of controlled breathing prior to the time of scanning. The aim of this design was to produce similar tidal volumes and respiratory frequencies as spontaneous breathing at rest. However, both inspiration and expiration during controlled breathing were divided into consecutive segments (2 in inspiration, 4 in expiration) with momentary pauses in respiration between each segment. A block design paradigm was used for each BOLD scan experiment, during which subjects alternated between 30 second periods of either spontaneous or controlled breathing, for a total of 8 periods. All experiments began with the spontaneous breathing period. The subjects received audible cues from the investigators on when to change breathing methods. All subjects underwent two scanning experiments. Functional images were processed using cross-correlation analysis by SPM99 software application. Pixels exceeding the threshold p value of <0.0001 were included in the maps of brain activation.

RESULTS

Image analysis demonstrated high intrasubject reproducibility upon repeat of experiments. Time-locked signal increases during controlled breathing periods were observed bilaterally in regions of the motor and sensorimotor cortices (Figure 1 A-C), supplementary motor areas, and cerebellar hemispheres. Similar signal increases were also observed in the pons and anterior cingulate gyrus. In two of three subjects, pixels with significantly decreased signal that temporally correlated with periods of controlled breathing were identified in the brainstem, near the level of the ponto-medullary junction (Figure 2 A-C).

CONCLUSION

A novel design of controlled breathing is presented here as a feasible technique for the functional imaging of neural respiratory control centers. The motor and sensorimotor cortex, supplementary motor area, and cerebellar activation depicted in the present study are in agreement with previously established techniques evaluating volitional breathing [1,2,3]. A primary improvement in the present study, however, is the obviation of the need for ventilation equipment or breath-hold techniques. Additionally, findings of decreased activation in the brainstem near the ponto-medullary junction have, to our knowledge, not been previously reported. Further studies are warranted to evaluate the ability of this single task technique to identify the neuroanatomic correlates of breathing and to determine the significance of their involvement with respiratory control.

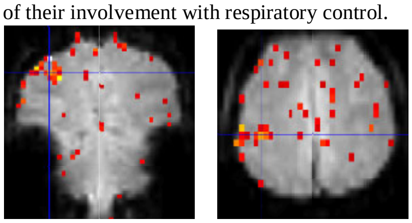

Figure 1A-1B: Representative activation maps in coronal (left image) and axial (right image) planes show a cluster of pixels (cross lines) with increased activation in the motor cortex.

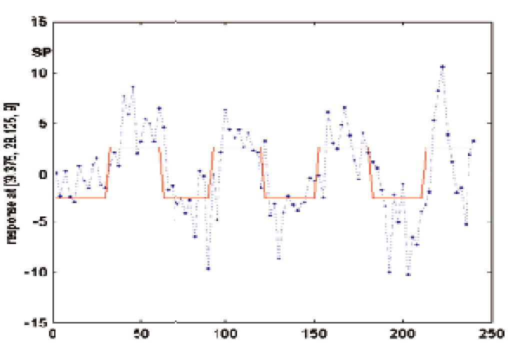

Figure 1C: Time course data graph from the pixels depicted in Figure 1A-1B shows increased activation correlating with onset of controlled breathing periods.

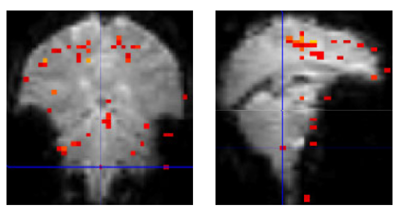

Figure 2A-2B: Representative activation maps in coronal (left) and sagital (right) planes show a small focus of activation (cross lines) near the ponto-medullary junction.

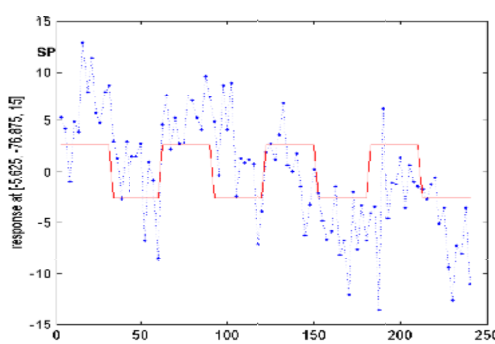

Figure 2C: Time course data graph from the pixels depicted in Figure 2A-2B shows the increased activation correlating with periods of spontaneous breathing. Decreased activation is seen during periods of controlled breathing.

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