VIII. 5. Human Study Regarding the Brain Responses to Respiratory Resistance

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The main role of respiration is to exchange oxygen and carbon dioxide through the lungs. It is controlled involuntarily by the respiratory center in the pons and voluntarily through the motor cortex. Dyspnea, shortness of breath or a subjective discomfort of breathing, usually associated with cardio-pulmonary diseases, occurs even in normal conditions during intense physical exertions, such as exercise or loaded breathing, or at high altitude. Respiration has an intimate relation to emotions. When angry, excited, fearful, or depressed, breathing takes a different pattern. The aim of this study was to localize anatomical sites of the brain of healthy subjects that were functionally altered by resistive inspiratory loaded breathing lasting for 30 minutes by using a brain imaging technique, PET and statistical parametric mapping1). Twenty-eight male normal volunteers with mean age of 30.2 years (SD 8.6) were included in this study. Respiratory resistance was made using an apparatus consisting of a semi-closed ventilation circuit with a unidirectional Hans-Rudolph valve2). Respiratory overloads were introduced by applying inspiratory resistance to the inspiratory port of the valve while subjects breathed through the valve. Thirteen subjects were studied during 30 cm H2O/L/sec inspiratory resistive loading (moderate task group), five subjects were studied during 70 cm H2O/L/sec inspiratory resistance (severe task group), and the other ten subjects were studied during resting breathing without resistance (control group). After breathing for one minute the restricted respiration task was performed during 30 minutes at each level of resistance, just after this the subjects rated the sensation of difficulty in breathing (dyspnea) using a modified Borg Scale3), ranking the magnitude of difficulty in breathing, from 0 (none) to 10 (maximal).
Relative regional cerebral glucose metabolism was measured with positron emission
tomography (PET; PT931 (CTI, Tennesee)) by using fluorine 18 (\(^{18}\text{F}\))-labeled
fluorodeoxyglucose (FDG). PET studies were carried out by injecting average 191.51 MBq
(SD 69.42) of FDG at one minute after applying the inspiratory resistance or during resting
breathing. Scanning was started at 30 minutes after injection of FDG. The posture was
kept supine throughout the examination run.

Image processing and statistical analyses were carried out using SPM99. This
procedure included anatomical standardization of a subject’s brain images to mach a
standard PET template (template of SPM99). The spatially transformed images were
smoothed using a $13 \times 13 \times 12$ mm at full width half maximum (FWHM) 3D-Gaussian Kernel.
The group comparisons were made using ANOVA and Student’s t-test adopting the
threshold of significance at $p < 0.001$, uncorrected for multiple comparisons. Group
comparisons showed extensive activations and deactivations. Inspiratory loads, both mild
and moderate, induced brain activations in the rectal gyrus, precentral gyrus and postcentral
gyrus (Figs. 1 and 2). Dyspnea induced activations in the bilateral rectal gyrus (Brodmann
area 11, Fig. 1) and the right temporal pole. Increases in glucose metabolism in the rectal
gyrus as well as in the amygdala (not activated in this study) have been reported in panic
disorder\(^4\,\,\,5\)\). The right temporal pole has been associated with respiratory rhythm\(^6\)\).
Activations of this area found in this study supported this hypothesis. Most of these areas
responded linearly with the level of respiratory resistance except the superior, temporal
gyrus, inferior frontal gyrus and middle temporal gyrus; these areas responded all or
nothing. Extensive metabolic reduction was found in the parietal–occipital brain areas with
the highest reduction in the right cingulate gyrus (Brodmann area 23, Fig. 2).

In conclusion respiratory distress activated the motor area, frontal lobe and
temporal pole bilaterally. These areas could be related to respiratory controls and emotion.
Extensive reduction in brain metabolism was found in the posterior part of the brain
including the parietal lobe

References
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Figure 1. brain activation by respiratory distress, comparison between group 30 minus control.

Figure 2. brain deactivation by respiratory distress, a comparison between control minus group 30.