Quantitative fMRI studies in rats during non-chemically based hypotension

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INTRODUCTION

BOLD changes are commonly used for studying functional brain activity [1]. The BOLD response is related to various physiological parameters, such as oxygen consumption, blood volume, blood flow and arterial hematocrit. If quantitative BOLD measurements [2] are not available, only modeling approaches can make mapping the brain activity with BOLD imaging reliable. Hence experimental results examining how systemic physiological changes (e.g., blood pressure) modify the BOLD response are needed. Prior studies have induced hypertension in rat using a drug (Norepinephrine or Nitroprussid) and studied the changes in BOLD and CBF changes during electrical forepaw stimulation [3]. Use of these drugs for hypertension experiments do not only vary the systemic pressure but also influence the behavior of cerebral arteries. Our aim was therefore to study the changes of the BOLD response in steps of non-invasively induced levels of arterial hypotension.

MATERIALS and METHODS

Animal preparation: Six artificially ventilated Sprague-Dawley rats were anesthetized by α-chloralose (40 mg/kg/hr) and *D*-tubocurarine chloride (0.5 mg/kg/hr, i.p.). An arterial line was used for monitoring blood pressure and taking samples for blood pH, pO_2, pCO_2 throughout the experiment. ***MRI measurements:*** All fMRI data were obtained on a modified 9.4T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^{1}H resonator coil for BOLD and CBF measurements [2]. Spin echo EPI data were acquired with TR of 2 s. The images were collected in matrix of 64×64 with slice thickness of 2 mm, and voxel resolution of ~0.15 μL. The slice position was selected at the level of Bregma. The hypotensive steps (of 100, 80, 60, and 40 mmHg) were maintained by a computer-controlled negative lower body pressure method (Fig. 1A) which has been described previously [5]. The duration of each hypotensive step was ~10 min and after each step the pressure was allowed to rise spontaneously. Data were collected in 90 s windows: 30 s before and after the 30 s forepaw stimulation (3 Hz, 2 mA, 0.3 ms) in every hypotensive step where both paws were stimulated separately.

RESULTS

BOLD responses observed on the contralateral side of the stimulus during hypotension steps are shown in Fig. 1B. The BOLD responses were measured only in those voxels where the Student t-statistics showed significant change with $P<0.05$. When comparing the BOLD response, there were no significant differences across the hypotensive steps of 100, 80, and 60 mmHg for baseline CBF levels, indicating autoregulation. However there was a significant drop in baseline CBF level at the hypotensive step of 40 mmHg, indicating break from CBF autoregulation.

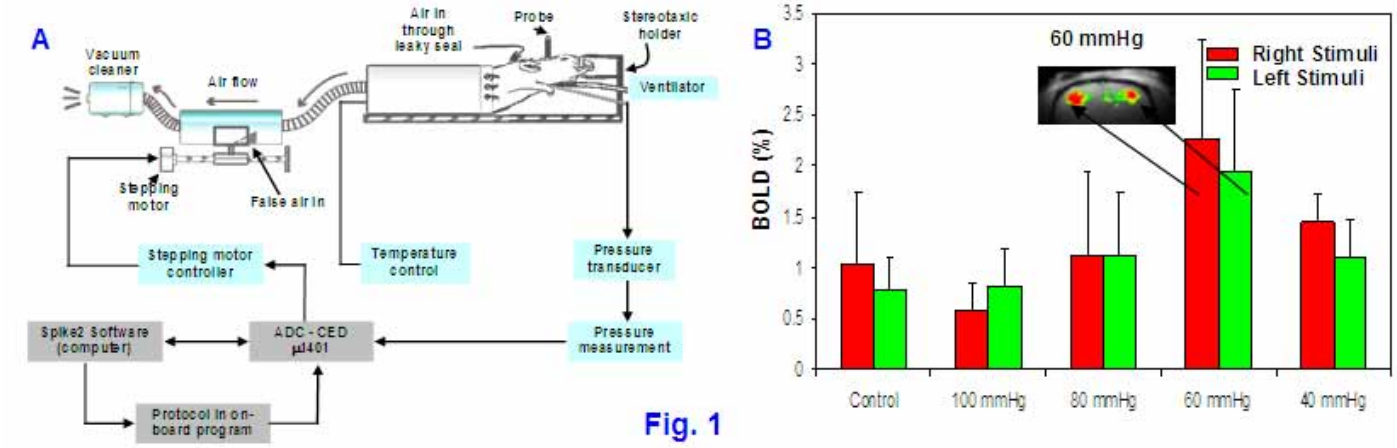

Fig. 1

DISCUSSION

Prior studies using chemically induced hypotension have found that the BOLD response to stimulation did not change during hypotension [3] despite concomitant changes in CBF and CBV produced by hemorrhagic hypotension within range of 40-70 mmHg [4]. While our results support these prior observations for the autoregulatory range of blood pressure, they also demonstrate that below the threshold of CBF autoregulation, the BOLD response is significantly higher than that of the control. These results indicate that change in blood pressure can influence the BOLD response. Consequently the BOLD response alone cannot be used to accurately monitor brain function in experimental settings when blood pressure drops below the threshold of CBF autoregulation.

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