Angiotensin II – but not norepinephrine and sodium nitroprusside – decreases the renal BOLD signal

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Introduction :

Angiotensin II (A2) has strong influence on sodium homeostasis and blood pressure regulation. These effects are partly mediated by renal hemodynamics. The available clearance techniques to assess A2 effects on renal hemodynamics are time consuming. Furthermore, diuresis has to be guaranteed by fluid infusions which may confound A2 effects. However, alternative non-invasive techniques to evaluate human renovascular responsiveness to A2 are missing so far. We here evaluate the potential of renal BOLD fMRI techniques to assess A2-induced renovascular responsiveness. Relative to their mass and metabolic capacity the kidneys are highly perfused. In consequence, the renal BOLD signal is determined by blood supply rather than oxygen consumption. Renal blood supply is autoregulated over a wide range of renal perfusion pressure. Renal autoregulation prevents changes in renal blood flow [1] in the presence of sodium nitroprusside (SNP)–induced decrease of arterial blood pressure and norepinephrine (NE)–induced increase of arterial blood pressure. A2 increases arterial blood pressure, too. However, the normal response of the renal vasculature to A2 is vasoconstriction with the result of reduced renal blood flow [2]. It was demonstrated in animal experiments, that BOLD MRI can detect changes in renal oxygenation during an acute reduction of blood flow [3]. Thus, we hypothesized that A2 reduces the renal BOLD signal. Other vasoactive substances (such as NE or SNP) are hypothesized to have no effect on this signal. In order to avoid motion artifacts and to obtain a good temporal resolution in the dynamic imaging study, a fast multi-echo EPI sequence was chosen.

Materials and Methods :

The study was approved by the local ethics committee. Six healthy male volunteers (age : 26 +/- 1.6 yrs. ; body weight : 71.2 +/- 9 kg ; mean +/- SD) participated. Prior to MRI studies all volunteers underwent an individual dose finding study. Beat-to-beat heart rate was assessed by convential single lead ECG. Continuous blood pressure was assessed non-invasively by Finapres-system. Data were recorded for 5 minutes (1 min. pre, and 4 min. post infusion). All vasoactive substances were titrated as to induce a 15 mmHg peak systolic blood pressure change (see Figure 1). Reflexive heart rate changes during the dose finding study are illustrated in Figure 2a. The same doses (A2: 8.8 +/-1.4 ng/kg ; NE : 52+/-12 ng/kg ; SNP: 2 ug/kg) were given during the MRI study. One MRI experiment consisted of six un-blocked randomized infusion sessions, each lasting 5 minutes. All three vasoactive substances were given twice. MR imaging experiments were performed at 1.5T on a Siemens Sonata using two elements of the spine array for signal reception. For BOLD imaging a multi-echo EPI sequence with the following parameters was used: matrix: 128x88, 4 slices, FOV: 30x21cm2, slice thickness: 5mm, 3 echo times: 40, 108 and 177ms. T_2* maps were calculated using a mono-exponential model and averaged over a cortex dominated ROI. During imaging the heart rate of the subjects was measured with a pulse oxymeter. As during the dose finding studies, there was one minute of baseline scanning prior to drug administration. MR acquisition was continued for the next 4 minutes.

Results :

Fig. 1 indicates that the dose finding study was sufficient. Fig. 2a and Fig. 2b show that heart rate changes induced by the vasoactive substances during the MRI study and during the dose finding study were similar, suggesting comparable underlying blood pressure changes during dose finding and during MR study. T_2* values measured during the administration of the vasoactive substances for one session of one subject are shown in Fig. 3. In our experiments, A2 caused a shortening of T_2* between 6% and 10%, whereas neither SNP nor NE lead to significant changes in the transverse relaxation time. For all drugs, a control ROI in muscle tissue did not show signal changes at the first echo time. Due to short transverse relaxation times, T_2* values could not be reliably calculated in the muscle tissue.

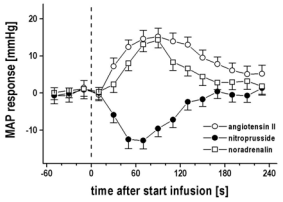

Fig1: Blood pressure after administration of vasoactive substances in dose finding study, averaged over all subjects.

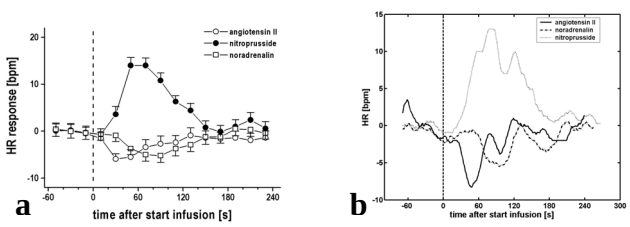

Fig2: Heart rate changes after administration of vasoactive substances in dose finding study averaged over all subjects (a) and for one subject during one session of the MRI experiment (b).

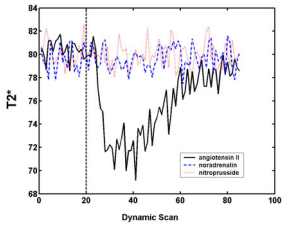

Fig3: T_2* evolution in the kidney after administration of the vasoactive substances.

Discussion :

As hypothesized A2 decreases the renal BOLD signal. This response is specific in two ways. First, the other vasoactive substances – although of equal potency concerning blood pressure responses – did not alter the renal BOLD signal. Second, control tissue (muscle) did not respond to A2. The method described here is suitable to assess A2-induced responsiveness of the renal vasculature and may thus be of great value in human hypertension research.

References :

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