Focused Ultrasound Stimulation of the Ventrolateral Periaqueductal Gray Decreases Blood Pressure in Spontaneously Hypertensive Rats

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Background, Motivation and Objective

Currently, increasing number of patients with primary hypertension develop resistant hypertension, which is untreatable with the majority of available antihypertensive drug therapies. Several device-based procedures such as catheter-based renal denervation or deep brain stimulation targeting the cardiovascular autonomic nervous system to treat resistant hypertension have made varying degrees of success but require invasive and complex surgery. We have shown previously (IUS 2018) that acute Ultrasound (US) transcranial neurostimulation of the ventrolateral periaqueductal gray in spontaneously hypertensive rats（SHR）can have antihypertensive effect. In this study, we aimed to evaluate the efficacy of chronic US stimulation during one week and to explore the potential mechanisms.

Statement of Contribution/Methods

We randomly divided 32 rats into 4 groups: Wistar-Kyoto (WKY) rats, SHRs, Experimental and Sham-treated (n=8 per group). In the Experimental group, transcranial focused US stimulation was targeted to the VLPAG of SHRs as the antihypertensive target for 7days. In the Sham-treated group, the SHRs were treated with the same procedure as the experimental group but no US stimulation. We then measured the systolic blood pressure (SBP) and mean arterial pressure (MAP) of all groups during one week. We also characterized the spatial distribution of US stimulation evoked neural activity using antibodies against c-Fos.

Results/Discussion

The SBP and MAP of SHRs increased over the one-week treatment period compared with WKY. In the Experimental group, US stimulation significantly decreased the SBP and MAP and caused significant differences with the Sham group. The c-Fos analysis indicated that US stimulation evoked the neurons both in VLPAG and in caudal ventrolateral medulla (CVLM) regions. The results demonstrate the antihypertensive effect of chronic compared to acute US stimulation of the VLAPG and the plausible involvement of the medulla blood pressure control center.

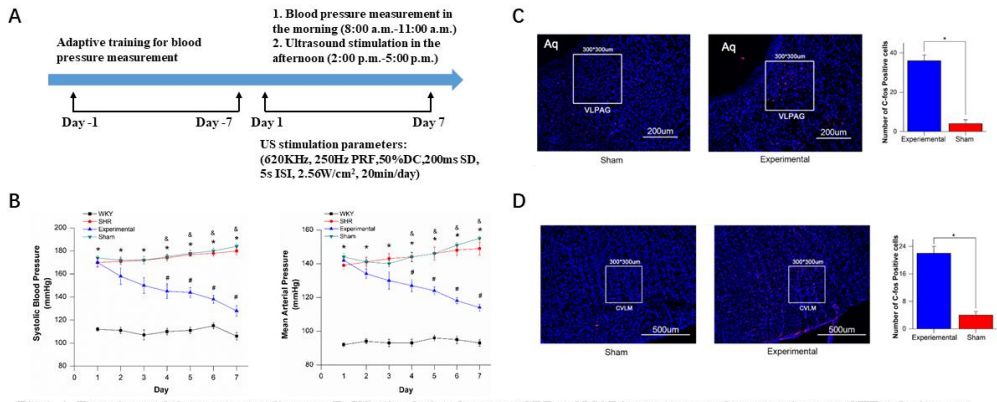

Fig.1. A. Experimental time sequence diagram. B. US stimulation decreases SBP and MAP in spontaneous hypertensive rats (SHRs) during one week. Values are given as the mean ± SEM of 8 animals per group. *SHRs versus WKY, #Experimental versus SHRs, and &Sham-treated versus Experimental, *P< 0.05 of each symbol at each time point in the Scheffe multiple-range analysis, respectively. C. The c-Fos expressing both in sham and experimental group in VLPAG. The 300*300 micrometer square (um²) white represents the region used for counting c-Fos positive cells. Values are given as the mean ± SEM of 8 animals in each group. * P < 0.05 of each symbol in the Student's t-test. D. The c-Fos expressing both in sham and experimental group in CVLM. The 300*300 micrometer square (um2) white represents the region used for counting c-Fos positive cells. Values are given as the mean ± SEM of 8 animals in each group. * P < 0.05 of each symbol in the Student's t-test.