Establishing the Coordinates to the RVLM in Wister Rats

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Introduction

Hypertension is becoming a global health concern. By 2025, the number of adults with hypertension is expected to increase by 60% to a total of 1.56 billion. Renovascular hypertension, a form of secondary hypertension, is characterized by unilateral renal artery stenosis. We use the Goldblatt model (2 kidney 1 clip) to establish this form of hypertension. This impairs the vasodilatation of the brachial artery and increases Angiotension II. Angiotension II is believed to be a major neurotransmitter in the Renin-Angiotension-Alloson system (RAAS) which increases ROS (reactive oxidative species) via activation of the NADPH oxidase. An increase in ROS is a marker for oxidative stress. "Enhanced production of ROS causes a loss of the bioavailability of nitric oxide, which impairs endothelium-dependent vasodilatation [2]."

Due to vasodilatation impairment via nitric oxide degradation, the Baroreflex sensitivity (BRS) is reduced in hypertension. Ultimately if we can enhance the availability of nitric oxide then we can increase the gain of the baroreflex and thus reduce blood pressure. The central circuitry involved in baroreceptor-mediated control of sympathetic outflow comprises of an excitatory projection from the NTS to CVLM, an inhibitory projection from the CVLM to the RVLM, and an excitatory projection from RVLM to pre-ganglionic sympathetic neurons [1]. The RVLM is one of the many regions in the brain which controls blood pressure. Baroreflex afferent nerves project to the NTS in the dorsomedial medulla.

Nitric oxide donors can enhance the availability of nitric oxide in the brain. In order to test any possible nitric oxide donors, we must first establish the correct coordinates to the RVLM. Unfortunately there is no consensus on where the RVLM is located. The RVLM has no clear boundaries and its location differs with strain, sex, age, and the weight of the rats. Nonetheless we used an atlas with anatomical landmarks such as the lambda as a comparison as well as computer generated coordinates for our testing. We then identified the region we target to be the RVLM by noting a cardiovascular response after the injection of glutamate.

Materials & Methods

Male Wister rats housed in a temperature controlled room with a 12:12 light/dark cycles. They were fed standard food and water. Rats between the ages of 8-12 weeks were used and were anesthetized with ketamine (100 mg/kg) and xylazine (10 mg/kg) injected intraperitoneally. After the surgery, the rats were monitored until they recovered. A histological analysis of the placement of the cannula was performed to verify these coordinates.

Objective

Identify a central RVLM location in a specific rat strain of similar weights

Results

The injection of glutamate caused an increase in pulse & blood pressure and a decrease in heart rate. Such an increase is expected because glutamate stimulates sympathetic activity within the nucleus of the RVLM. A decrease in heart rate can be explained due to the fact that the control centers in the RVLM will try to move the body towards homeostasis after a glutamate stimulus.

Therefore, the heart rate is decreased so that the pulse and blood pressure can revert to its original levels.

Conclusion

A microinjection to the RVLM at the following coordinates from the lambda: 3.4 caudal, 1.8 from the midline, & 6.5 ventral are plausible coordinates for Wister rats.

A histological analysis of the placement of the cannula above the RVLM will have to be performed in order to verify these coordinates.

References


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