Optogenetic Activation of OVLT Neurons Stimulates Water Intake and Produces a Sympathetically-Mediated Increase in Arterial Blood Pressure

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The organum vasculosum of the lamina terminalis (OVLT) plays a pivotal role in body fluid homeostasis and arterial blood pressure (ABP) regulation. The OVLT lacks a complete blood-brain-barrier and responds to an array of circulating factors such as NaCl and angiotensin II. Lesion of the anteroventral third ventricular region which includes the OVLT attenuates or reverses several forms of salt-sensitive hypertension. However, there is limited evidence to demonstrate that direct activation of OVLT neurons alters body fluid homeostasis or elevates ABP. To address this question, Male-Sprague-Dawley rats (300-350 g) received an injection of rAAV9-CamKII-hChR2(H134R)-EYFP (10^{12} particles/mL, 200nL) into the OVLT. A fiber optic cannula (200µm) was implanted 300µm dorsal to OVLT. Approximately 2-3 week later, optogenetic activation of OVLT neurons (10ms pulse, 50% duty cycle, 30 min) produced frequency-dependent increases in water intake (1Hz: 1.0±0.5mL; 5Hz: 4.2±0.6mL; 10Hz: 8.0±1.8; 20Hz: 10.2±2.1mL, n=4, P<0.05). In separate experiments, optogenetic activation of OVLT neurons produced a frequency-dependent increase in mean ABP (1Hz: 1±1 mmHg; 5Hz: 3±1mmHg; 10Hz: 7±1mmHg; 20Hz: 13±1mmHg, n=4, P<0.05) and heart rate (1Hz: 3±6 bpm; 5Hz: 15±5bpm; 10Hz: 40±12 bpm; 20Hz: 62±14bpm, n=4, P<0.05). Pretreatment with the vasopressin antagonist Manning Compound (10ug/kg, IV) did not affect these responses. However, pretreatment with the ganglionic blocker chlorisondamine (5mg/kg, IV) abolished the pressor (20Hz: 1±1 mmHg, P<0.01) and tachycardic (20Hz: 4±7 bpm, P<0.05) responses to activation of OVLT neurons. Finally, in vivo single-unit recordings demonstrate that optogenetic activation produced frequency-dependent increases in cell discharge of OVLT neurons responsive to either intracarotid injection of hypertonic NaCl (0.3M NaCl, 50µL over 10 s, n=6) or angiotensin II (100ng over 10s, n=3). Collectively, these data provide evidence that direct activation of OVLT neurons stimulates thirst and produces a sympathetically-mediated increase in ABP.

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