Manganese-enhanced MRI (MEMRI) imaging reveals elevated sodium intake induced by deoxycorticosterone acetate (DOCA) modulates activity in select brain regions in male SD rats

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Introduction: Excessive intake of sodium is linked to cardiovascular disease. Activation of the renin-angiotensin-aldosterone system is the most common mechanism underlying an increase in sodium seeking or sodium appetite. Numerous brain regions are known to be excited or inhibited during the activation of sodium appetite.

Objective: To determine whether new brain regions linked to chronically elevated sodium intake could be uncovered using novel brain imaging techniques.

Material and Methods: Male SD rats received either a subcutaneous pellet of the aldosterone precursor deoxycorticosterone acetate (DOCA, 150 mg/60 day release) or sham surgery (n=6-8/group). Following surgery, all animals had access to both normal water and a 1% NaCl, 0.2% KCl solution. Between 11-13 days post-surgery the average daily sodium intake in the DOCA group was 196±21 versus 21±4 ml in the control group. On day 14 post-surgery all animals were given an intraperitoneal injection of manganese chloride (25 mg/kg). Following 24 hrs of recovery, while lightly anesthetized, the brain of each animal was imaged on a 4.7 Tesla MRI using a multi-slice spin echo sequence: TE=15ms, TR=350ms, 22 slices, 256x256 resolution. MEMRI enabled mapping of signal enhancement or depression in the brain associated with neuronal activity marked by paramagnetic Mn2+ accumulation.

Results: Preliminary results suggest an overall decrease in activity within many brain regions of interest in the DOCA/salt animals versus controls. Regions with significantly reduced activity following DOCA/salt treatment ($P<0.05$) included the shell of nucleus accumbens, the hypothalamic dorsomedial nucleus, and dorsal raphe. There was also a strong trend for a reduction in activity in both the ventral tegmental area and the ventral posteromedial thalamic nucleus ($P<0.07$). Many of these areas are linked multiple facets of sodium appetite/intake, including autonomic and defensive behavior control (dorsomedial hypothalamus), foraging (ventral tegmental area, nucleus accumbens),

orofacial control (ventral posteromedial nucleus of the thalamus) and behavioral state (dorsal raphe).

Conclusions: These findings suggest that free sodium access during elevated sodium-appetite suppresses activity in multiple brain regions. These preliminary results also identify potential new targets for therapeutic intervention to control sodium intake.

Keywords: Manganese-enhanced MRI, sodium intake, deoxycorticosterone acetate, brain activity, rats

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