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QUANTITATIVE MEASUREMENT OF CEREBRAL BLOOD FLOW USING ARTERIAL SPIN LABELING IN WOMEN WITH OVERACTIVE BLADDER

Hypothesis / aims of study

This is the first study to investigate changes in cerebral perfusion using arterial spin labeling in subjects with overactive bladder (OAB). Arterial spin labeling (ASL) is a fMRI technique that uses inverted proton spins of magnetically labeled water in the blood as a tracer to quantitatively and non-invasively measure cerebral perfusion. Our aim is to determine whether CNS processing of sensory information differs between women with OAB and healthy controls. Our hypothesis is that OAB is associated with quantitative increase in cerebral perfusion in select regions of interest in women with OAB as compared to controls.

Study design, materials and methods

Cerebral perfusion was measured in 12 women with OAB and 10 healthy female controls using arterial spin labeling (ASL) fMRI. All women underwent two imaging studies using a pseudocontinuous ASL sequence: 1) on an empty bladder and 2) on a full bladder when experiencing urinary urgency using an oral fill protocol. We selected ROIs in the brain a priori based on the existing literature of OAB and interstitial cystitis (Ref.1-3). Absolute regional cerebral blood flow (rCBF) for each ROI for each subject was calculated. We compared 1) rCBF at baseline (empty bladder state) between OAB and control groups 2) rCBF in the empty bladder state to rCBF in full bladder state within each group (OAB and controls) and 3) change in rCBF (from empty to full bladder) in the OAB group to change in rCBF in the control group. We also performed secondary non-hypothesis driven whole-brain analysis using SPM to evaluate for rCBF pattern changes between empty and full bladder states.

Results

There was no significant difference in the median age of the OAB (52.5±16) and control (45.1±11.5) groups. The median anxiety and depression scores were low for both groups.

At baseline, in the empty bladder state, women with OAB had significantly greater absolute rCBF than controls in the right thalamus, left thalamus, pons/midbrain area, and right and left supplemental motor area (SMA) (Table 1). Figure 1 shows the group activation map of regions that showed greater perfusion at baseline in women with OAB than controls.

In the OAB group, rCBF (ml/100g/min) in the full bladder state was significantly higher in the full bladder state as compared to empty bladder state in right ACC (49.52±1.49 vs. 44.56±0.59, P < .05), left ACC (54.02±1.46 vs. 49.29±0.85, P <.05) and left insula (54.99±1.09 vs. 50.46±1.72, P <.05) (Fig. 2 & Table 2). There were no significant differences in rCBF between the full and empty bladder states in the control group (Fig. 2 & Table 2).

The change in absolute rCBF from empty to full bladder state in the right ACC, right DL PFC and left thalamus was significantly greater in the OAB group than the control group (Table 2).

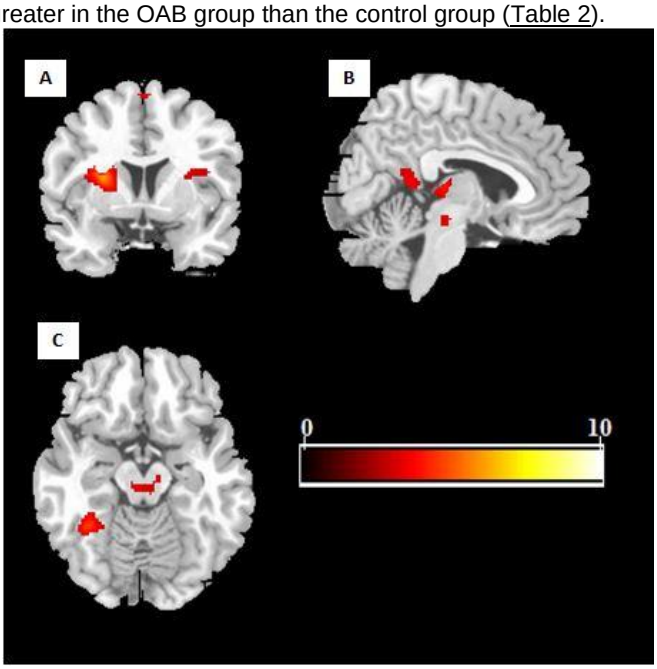

Figure 1: ROI showing activations at baseline in OAB as compared to controls. A: Suppl. motor area (SMA) (0,4, 66) and thalamus; B: thalamus (-8, -26, 8 and 14, -32, 10); C: pons/ midbrain (-4, -24, -16). Figures in parenthesis are xyz co-ordinates of peak activity.

ROI	OAB	Controls	P-value
R thalamus	46.46± 1.51	55.96±2.58	.004**
L thalamus	45.48± 1.46	53.99±2.08	.003**
Pons/midbrain	40.07± 2.83	53.32±2.86	.004**
R SMA	39.72± 1.04	46.61±2.84	.029*
L SMA	40.42± 0.90	49.09±3.03	.01*

* P < .05** P < .01

Table 1: Absolute rCBF (ml/100mg/min) in OAB vs. controls at baseline in the empty bladder state

Figure 2: absolute rCBF for each ROI in empty and full bladder for OAB and control groups.

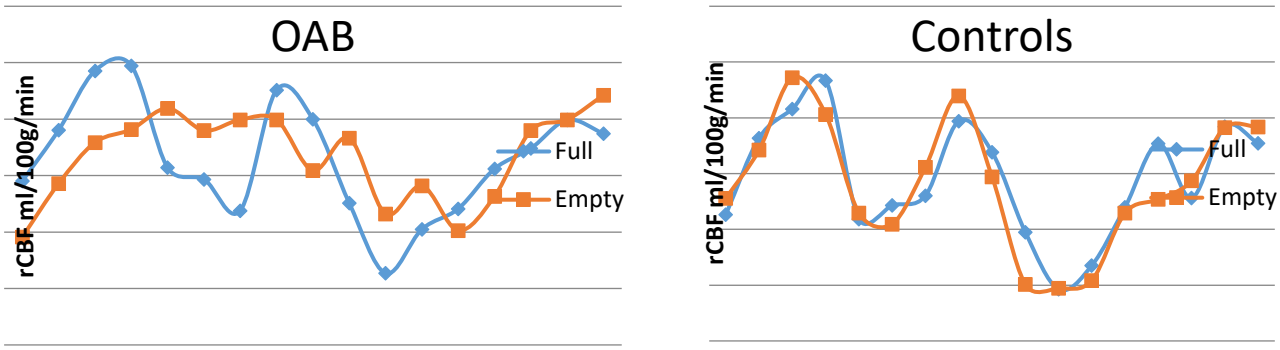

Table 2: Change in absolute rCBF in select ROIs in OAB and healthy controls

ROI	**OAB group (ml/100g/min)**		**Controls (ml/100g/min)**	
	Δ (Full-Empty)	Change (%)	Δ (Full-Empty)	Change (%)
Rt. ACC	**4.96±1.79***	**11.4%**	**-1.45±1.61†**	**-2.40**
Lt. ACC	**4.73±1.69***	**9.9%**	1.07±2.20	2.94
Rt. Dl PFC	6.35±3.22	14.3%	**-2.79±1.88†**	**-7.25**
Lt. Dl. PFC	5.65±2.79	12.2%	3.03±3.34	7.63
Rt. thalamus	-5.25±2.67	-8.0%	-0.53±2.99	-0.24
Left thalamus	-4.31±2.28	-6.9%	**1.69±1.96†**	**4.43**
PCC	-8. 06±4.58	-12.6%	-2.56±3.38	-2.13
Rt. insula	2.64±1.74	5.5%	-2.28±2.51	-2.69
Lt. insula	**4.53±1.64***	**9.9%**	2.21±1.51	5.46
Pons/midbrain	-5.75±5.17	-7.4%	4.69±3.60	17.97
Rt. SMA	-5.26±3.69	-11.2%	-0.09±1.83	-0.04
Lt. SMA	-3.85±2.00	-7.8%	1.34±2.48	3.45

* P < .05 paired t-test comparing rCBF in full to empty bladder within OAB group
† P < .05 independent t-test comparing change in rCBF in OAB and control groups

Interpretation of results

At baseline, even in the empty bladder state, women with OAB show greater cerebral perfusion (increased neural activity) in the thalamus, pons/midbrain area and SMA than controls. Activation of the thalamus and the pons/midbrain area in the empty bladder state suggests presence of increased afferent signalling in women with OAB as compared to controls. Greater activity of the SMA in OAB group may represent pelvic floor muscle activity to protect against incontinence until a socially acceptable place to void is reached.

In women with OAB, urinary urgency is associated with 10-14% increase in cerebral perfusion in key regions of the brain that process anxiety i.e. the dorsal ACC and the insula.

Our finding that changes in rCBF in response to bladder filling can be quantitatively measured suggests that cerebral perfusion could potentially be used as an objective biomarker for OAB.

Concluding message

The brains of women with OAB show evidence of increased afferent signalling at baseline. In women with OAB, urgency is associated with further quantitative increase in cerebral perfusion in regions known to process anxiety (limbic system). Cerebral perfusion changes quantitatively in response to bladder filling and is a potential objective biomarker for OAB.

References

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Disclosures

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