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ASSESSING NORMAL AND ABNORMAL BLADDER CONTROL USING FUNCTIONAL MRI AND RESTING STATE CONNECTIVITY MRI(RS-FCMRI).

Hypothesis / aims of study

The aim of this study is to identify differences in brain activity and functional connectivity between women with normal bladder function and those with urgency urinary incontinence. We hypothesize that there will be a significant difference in fMRI activation pattern of previously identified supraspinal bladder control network regions between women with normal bladder functions and those with urgency incontinence (e.g., dorsal anterior cingulate, bilateral anterior insula, orbitofrontal cortex). We hypothesize that these regions will overlap with known regions involved in executive control, default mode network, limbic system and sensory motor regions. We hypothesis that compared to women with normal bladder function, women with urgency urinary incontinence will show decreased functional connectivity between regions identified by fMRI and known networks that support cognitive, sensory motor and control functions.

Study design, materials and methods

This is a cross-sectional prospective study comparing brain imaging using fMRI and rs-fcMRI in women with normal bladder function(control) and those with daily urinary urgency incontinence with urodynamic evidence of detrusor overactivity (cases). Participants were women between ages 40-65. Urinary symptoms were documented with a 3-day diary and International Consultation on Incontinence Questionaire(ICIQ-SF). MRI acquisition was performed using a Siemens Magnetom Tim Trio 3.0 Tesla scanner (Erlangen, Germany) with a twelve-channel head coil. Blood-oxygen level dependent (BOLD)-weighted functional imaging were collected in an oblique plane (parallel to the ACPC line) using T2*-weighted echo-planar imaging covering the whole brain. FMRI was obtained with repetitive bladder filling and emptying during scanning. Each subject underwent two blocks with relatively empty bladder and 2 blocks with bladder filled to capacity. Each block includes 4 repetitions (runs) of infusion and withdrawal of fluid. Rs-fcMRI images were obtained at rest with empty and full bladder

Results

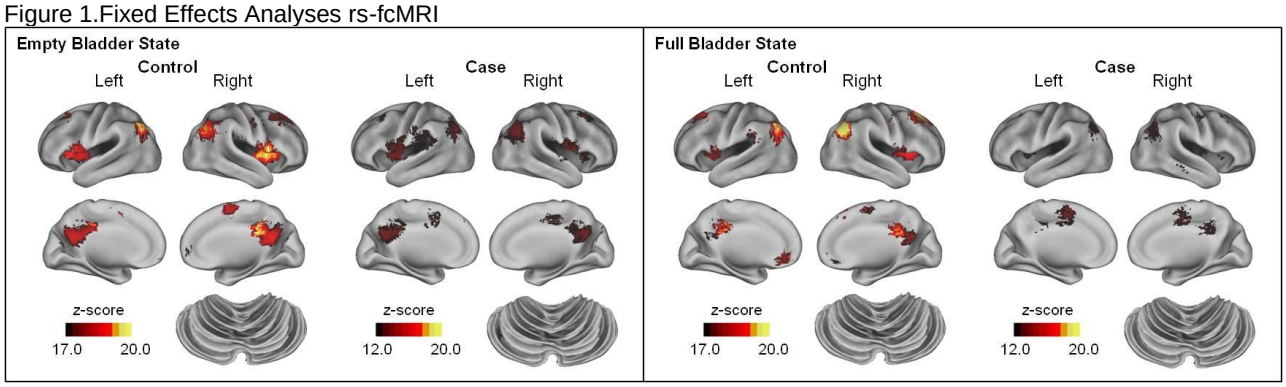
A total of 19 controls and 11 cases participated in this study. The two groups did not show any significant differences in age, BMI, number of vaginal deliveries or amount of fluid intake. There were significant differences in number of urgency leakage ($p<0.01$), nocturia episodes($p=0.02$) ,urinary frequency ($p<0.01$) and ICIQ-SF score. fMRI data obtained with subtle bladder filling and emptying phases (main effect of time) identified 28 regions of interest with significant change in BOLD signal (see table 1). Additionally, 8 regions of interest were identified that showed significant difference between empty and full bladder states (Bladder state by time). Rs-fc fMRI data shows that as bladder is filled to capacity, there is a significant change in connectivity of regions of interest identified by fMRI to the rest of the brain (see Figure 1). In control subjects, a decrease in connectivity was observed to posterior cingulate while this reduction was not observed in the cases. Similarly, connectivity of the insula decreased as bladder was filled to capacity in the controls while this decrease was not significant in cases. The control subjects showed an increase in connectivity to anterior cingulate and middle frontal gyrus as bladder was filled to capacity while the there was no significant connectivity of these regions at empty or full bladder states in the cases.

Table 1.

Main Effect of Time	**X**	**Y**	**Z**	**Main Effect of Time**	**X**	**Y**	**Z**	**Bladder State x Time**	**X**	**Y**	**Z**
Postcentral Gyrus	36	-27	48	Insula	-47	7	6	Sup. Parietal	25	-50	64
Inf. Parietal	-50	-43	44	Sup. Temporal Gyrus	52	0	5	Precuneus	12	-57	62
Inf. Parietal	46	-47	41	Insula	43	0	4	Postcentral Gyrus	42	-26	42
Supramarginal Gyrus	50	-42	33	Sup. Temporal Gyrus	61	-7	4	Inf. Parietal	-47	-35	40
Supramarginal Gyrus	-52	-50	33	Inf. Frontal Gyrus	47	23	2	Ant. Cingulate	-04	13	-06
Supramarginal Gyrus	-54	-40	32	Ant. Cingulate	-6	27	-1	Post. Lobe Cerebellum	-18	-64	-18
Cingulate	-5	-31	30	Ant. Cingulate	1	20	-2	Ant. Lobe Cerebellum	-27	-58	-23
Mid.Temporal Gyrus	46	-70	23	Ant. Cingulate	9	33	-11				
Precuneus	-9	-62	18	Inf. Frontal Gyrus	-45	18	-11				
Sup. Frontal Gyrus	-19	50	17	Cerebellum – Culmen	-21	-58	-22				
Medial Frontal Gyrus	-9	50	12	Cerebellum –Ant. Lobe	21	-39	-23				
Putamen	26	-15	12	Cerebellum- Uvula	-18	-75	-24				

Claustrum	-30	-1	10	Cerebellum- Ant. Lobe	33	-48	-30				
Claustrum	33	6	9	Cerebelleum - Pyramis	-23	-70	-34				

Figure 1.Fixed Effects Analyses rs-fcMRI



Interpretation of results

Regions of interest showing significant differences in fMRI activation between controls and cases as bladder is filled to capacity were limited to anterior cingulate, inferior parietal, superior and inferior frontal gyrus. This could be partly because our participants were generally older (mean age of 56, range 40-64) which is consistent with previous report that brain responses to bladder filling decline with age either due to decrease in afferents or brain's responsiveness with aging. More interestingly however, functional connectivity findings show that there is a significant increase in connectivity of these regions of interest as a whole to control regions such as the cingulate and middle frontal gyrus in women with normal bladder function while this connectivity is missing in women with urgency incontinence. Furthermore, there is decreased connectivity to emotional processing.

Disclosures

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