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Khavari R[1], Karmonik C[1], Boone T[1]
1. *Houston Methodist Hospital*

SUPRASPINAL CONTROL VARIATIONS IN PATIENTS WHO VOID SPONTANEOUSLY VERSUS PATIENTS WITH VOIDING DYSFUNCTION IN WOMEN WITH MULTIPLE SCLEROSIS

Hypothesis / aims of study

Normal voiding is triggered by release of tonic inhibition from suprapontine centres, allowing the pontine micturition centre to trigger the voiding reflex. In this study, we seek to compare brain activity processes at the time of initiation of voiding in Multiple Sclerosis (MS) patients who are voiders versus patients with voiding dysfunction. We hypothesize that female MS Patients with voiding dysfunction have a distinct Blood Oxygen Level Dependant (BOLD) pattern activation in specific *a priori* regions of interest (ROIs) at the time of initiation of voiding when compared to female MS patients who void spontaneously.

Study design, materials and methods

Twenty seven ambulatory (with or without assistance) female patients with MS and lower urinary tract dysfunction were recruited for this IRB approved study. Patients were divided to two groups. Group 1; voiders (n=15) and group 2; voiding dysfunction (n=12) which included patients with postvoid residual of ≥ 40% of their maximum cystometric capacity or the ones who performed self-catheterization. We recorded brain activity via fMRI with simultaneous UDS. After motion correction, the Generalized Linear Model created individual fMRI activation maps at initiation of voiding. A high-resolution structural scan of the brain transformed the individual fMRI activation maps into Talairach space. From these transformed datasets, average fMRI activation maps (student t-test) for both groups were created separately, from which areas of significant activation were identified ($p<0.05$). *A priori* ROIs identified by a meta-analysis to be involved in the micturition cycle were identified in the pontine micturition centre (PMC), periaqueductal grey (PAG), reticular formation, cingulate, midbrain, thalamus, and prefrontal cortex. Average BOLD activation was determined and compared between groups.

Results

Group-averaged BOLD activation maps indicated distinct differences in activation patterns between groups (figure 1a). ROI analysis yielded consistent areas of increased BOLD signal activation in all ROIs group 1 compared to group 2 except in the left cerebellum (figure 1b, p-value < 1.5e-4). A reversed (negative) BOLD effect was noted in the PMC, PAG, left cingulate, left thalamus and the reticular formation.

Interpretation of results

Lower urinary tract has two functions: storage and voiding. Voiding symptoms (hesitancy, incomplete bladder emptying, and urinary retention) are common in MS, occurring in 34% to 79% of patients.[1] The switch between storage of urine to initiation of voiding and the control over this switch in located in the brain. Despite extensive research in the pelvic floor and the bladder, supraspinal centers and their role in initiating or modulating voiding in patients with neurogenic or nonneurogenic voiding dysfunction have not been studied. To our knowledge this is the first study to investigate the differences and similarities of brain regions involved in initiation of voiding in ambulatory MS patients.

Investigation in the higher neural control of micturition using functional neuroimaging thus far shows that the initial afferent stimulus comes from the sensation in the bladder as “strong desire to void”. Afterwards, the forebrain determines a person’s social circumstance and whether to proceed with voiding. Once it is socially acceptable to void, canters in the brain and spinal cord coordinate to produce bladder contraction and urethral sphincter relaxation.[2] In order for the pontine micturition centre (PMC) to begin micturition, visceral sensations from passive filling in the bladder are transmitted to the periaqueductal gray (PAG) of the brainstem and higher centres including thalamus, insula, and anterior cingulate gyrus. Other neural structures associated with the voiding reflex are the motor prefrontal cortex, supplementary motor cortex, and parahippocampus. Earlier positron emission topography studies have identified right dorsomedial pontine tegmentum and the right inferior frontal gyrus to be associated with significantly increased blood flow in healthy women at the time of voiding.[3] Our fMRI BOLD signal analysis results are consistent with these preliminary data in the literature where PMC, PAG, left cingulate, left thalamus and the reticular formation seem to have different pattern of activation between female MS voiders and the ones with voiding dysfunction. All of these structures may be involved during PAG activation to transmit input to the PMC to initiate micturition.

Concluding message

Our preliminary group and network analyses demonstrate that distinct patterns of activation and deactivation exists between MS patients who are voiders and who have voiding dysfunction. Exploring brain areas in patients with Multiple Sclerosis with voiding dysfunction is important to discern any altered control over the micturition cycle.

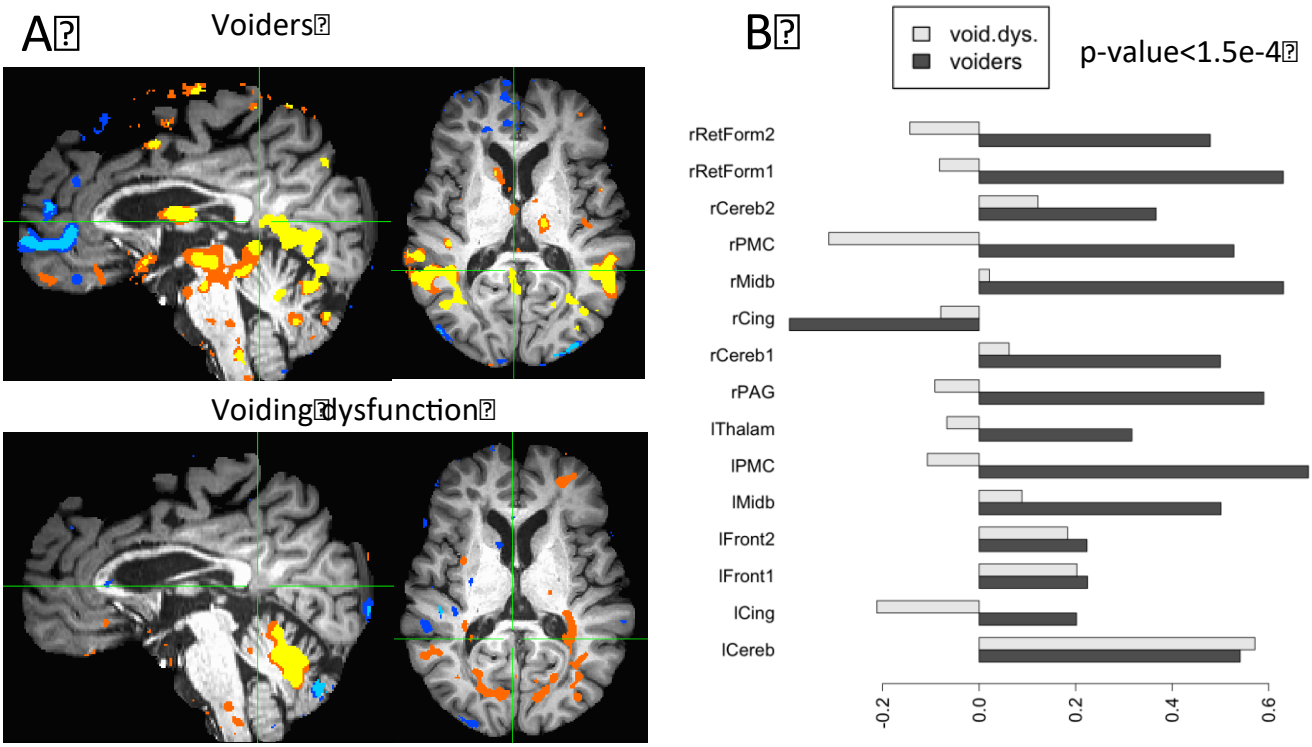

Figure 1: A: Group-averaged fMRI BOLD activation patterns for MS patients without and with voiding dysfunction. Distinct differences in both patterns can be appreciated. B: Average BOLD activity in selected regions of interests (ROI) derived from the BOLD maps in A. A predominant higher BOLD effect is observed for patients without voiding dysfunction (p<1.5e-4). Reverse (negative) of BOLD effect is noted in selected ROIs (Cereb: cerebellum, Cing: cingulate, Front: prefrontal cortex, Midb: midbrain, PMC: pontine micturition center, Thalam: thalamus, PAG: periaqueductal gray, RetForm: reticular formation)

References

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Disclosures

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