Brain Activation in Overactive Bladder Patients Evaluated by Pharmacological fMRI

S. Moonat[1], M. Pontari[2], S. Lebovitch[2], B. Lebed[2], M. Ruggieri[2], S. H. Faro[3], and F. B. Mohamed[3]

[1]Electrical Engineering, Temple University, Philadelphia, PA, United States, [2]Urology, Temple University, Philadelphia, PA, United States, [3]Radiology, Temple University, Philadelphia, PA, United States

Background and Objective

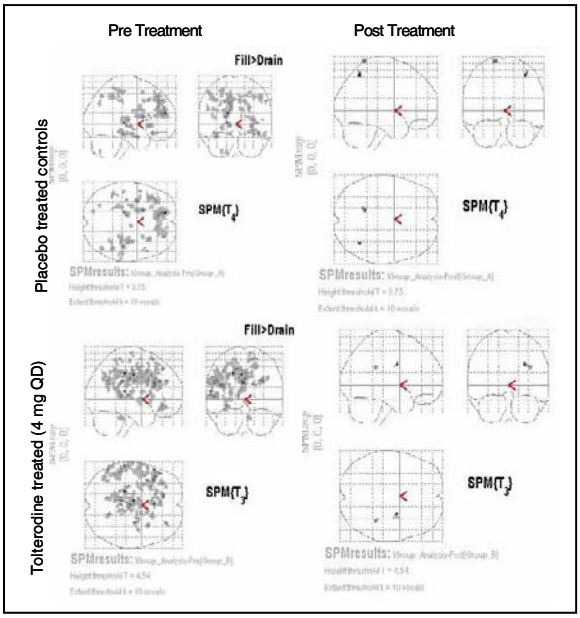
Overactive bladder (OAB) is considered to be a disorder of the urinary bladder and is defined by the International Continence Society Terminology Committee as "urgency, with or without urge incontinence, usually with frequency and nocturia" [1]. OAB patients experience urinary frequency and urgency, which is thought in part to be due to a dysfunction of the storage properties of the bladder, or a local alteration in bladder sensation. There is some preliminary evidence using functional magnetic resonance imaging (fMRI) that the brain response to bladder filling in OAB patients is abnormal [2,3]. The purpose of this work is to determine whether there are CNS differences in modulating bladder function that contribute to, or are themselves the cause of the symptoms in OAB patients. We further investigated the pharmacological fMRI changes using anticholinergic treatment of these patients with OAB. To our knowledge the mechanisms of anticholinergic drug induced changes of OAB symptoms at sites outside of the bladder has not been investigated using fMRI.

Methods & Materials

The experiments were performed on 9 female patients using a standard 1.5T GE imager. OAB patients were recruited from the urology clinic at our institution and informed consents approved by the Institutional Review Board were obtained. The primary eligibility requirement for study patients was greater than 8 voids per day based on a 24-hour voiding diary. All patients were required to stop taking any anticholinergic medications for a 2-week washout period prior to the baseline fMRI study. Initially a 16 Fr Foley catheter is placed into the bladder of the patient outside the scanner along with a separate 7 Fr dual lumen catheter that allows for both bladder filling and measurement of intravesical pressure during the fMRI procedure. Bladder pressure will be recorded using a portable urodynamics system located outside MRI scanner area (Delphis™ IP, Laborie Medical Technologies, Williston, VT). Initially a high resolution T1-weighted spin echo sequence (TR=500ms; TE=14ms) was used to acquire 37 contiguous axial images aligned parallel to the AC-PC line covering the entire brain using a 8-channel head coil. Imaging parameters were: matrix size = 256*256; TR (repetition time) = 600 ms; TE (echo time) = 15 ms; FOV (field-of-view) = 22 cm; NEX (number of excitations) = 1; and slice thickness = 4mm. Next, functional images were acquired with echo planar free induction decay (EPI-FID) sequences in the same plane as the structural images in an interleaved order. The functional imaging parameters will include: 64*64 matrix; FOV = 22 cm; slice thickness = 4mm; TR = 3 s; and TE = 54 ms. Patients were asked to keep the head still and keep the eyes closed throughout the scanning. The functional MRI experiment used a box-car type block design for collecting images. Scanning was performed at baseline prior to filling for 45 seconds. Normal saline is instilled into the bladder at a medium fill rate of 50 ml/min. Filling was stopped once the patient experiences the sensation of strong desire to void/and or urgency. The bladder will remain full for 30 seconds and another scan was performed. The bladder was then drained of saline. The completely drained bladder was again scanned for 30 seconds before another filling cycle. 10 volumes of EPI images were acquired for each fill and drain conditions. The fill/drain cycle was repeated a total of 5 times. After the last empty bladder scan is completed the catheter is removed and then an additional empty bladder scan is performed for 45 seconds with the catheter removed. Of the 9 patients recruited in this study fMRI data was collected on 4 patients before and 4 weeks after anticholinergic therapy with tolterodine (Detrol LA, 4 mg/day) and 4 patients before and after 4 weeks of placebo treatment. The data was then analyzed using SPM2 software and statistical parametric maps (SPM{t}) were generated to show visual representation of the areas in the brain wherein statistically significant differences in BOLD contrast between the full and drain conditions as well as between the control and the treatment groups.

Results & Conclusion

These results suggest that there may be unique area(s) in the brain modulated by bladder control in OAB patients that can be measured using fMRI. Based on group analysis on all the 9 patients prior to treatment our results show 15 statistically significant ($p<0.01$, extent threshold = 10) brain regions to be involved in the process of urge to void. They are as follows: A. superior anterior putamen, B: thalamus, C: anterior subinsular cortex, D: inferior lateral frontal, E: medial mid frontal, F: anterior mid frontal, G: anterior medial frontal, H: medial posterior mid frontal, I: mid lateral frontal, J: mid medial frontal, K: mid superior frontal, L: anterior superior frontal, M: frontal anterior medial, N: frontal mid medial, and O: frontal anterior lateral. Several of these areas such as the putamen, subinsular cortex and thalamus have been identified in previous investigations [2, 3]. A preliminary comparison of the effect of a 4-week course of treatment with placebo (N=4 patients) versus 4 mg QD tolterodine (N=4) is shown in the figure on the right. Overall these results show that there appears to be less urgency induced brain activation after treatment than before both for the active drug treatment as well as the placebo controls. It is not clear whether this represents an effect of the treatment or placebo. These preliminary results are encouraging and warrant further investigation with a larger patient population.



References: (1) Abrams P, et al. Neurourology & Urodynamics. 2002;21(2):167-78. (2) Pontari MA, et al. Neurourology & Urodynamics. 2000;19(3):323-64. (3) Griffiths D, et al. Journal of Urology. 2005 Nov;174(5):1862-7.