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CEREBRAL CONTROL OF BLADDER FUNCTION: THE BRAIN-BLADDER CONNECTION

Aims of Study

In urge incontinence, urodynamic investigation typically reveals detrusor overactivity. Treatment is then targeted at the detrusor, usually without knowledge of etiology and with variable success. Urge incontinence and detrusor overactivity, however, indicate an inability of the brain to volitionally control the voiding reflex. Functional brain imaging may offer new understanding of normal and abnormal bladder control and, ultimately, improved treatment.

Previous work, including functional imaging of the human brain by positron emission tomography (PET), has identified many brain regions concerned with normal bladder filling and voiding, but their functions remain unclear. To identify brain regions specifically involved in failure of bladder control, we compared brain activation in subjects with and without detrusor overactivity, monitored by cystometry, during functional magnetic resonance imaging (fMRI). fMRI is a rapid brain imaging technique that can monitor changes associated with detrusor contraction. Its hostile magnetic environment and low signal-to-noise ratio however present technical challenges.

The aims of this study were thus: to prove the feasibility of combining brain fMRI with simultaneous urodynamics; to delineate brain behavior during bladder filling; and to seek differences in brain response to bladder filling among subjects with and without detrusor overactivity. This abstract reports results from the first few subjects.

Methods

Subjects were of either sex, older than 20 y, and without evident neuropathy. Bladder control problems were not an exclusion criterion. After comprehensive assessment, including dual-channel urodynamics, scanning was performed with the subject supine in a 3T GE machine, using a standard head coil. Following structural imaging, a spiral scanning protocol was used to determine blood-oxygen-level-dependent contrast, representing neuronal activity. The whole brain was scanned once every 1.5 s, at a resolution of approximately 3 mm, while intravesical pressure was measured and saline solution was pumped in or out of the bladder through two 8-French transurethral catheters, connected via 10-meter stiff-walled tubes to remote urodynamic equipment. Strong desire to void was signaled by push button. Abdominal pressure was not measured, as it varied little and bladder behavior was already known.

To improve the signal-to-noise ratio, repeated blocks of imaging and measurements were performed. Each block started with 10.5 s rest, followed by rapid infusion of 30 ml saline into the bladder in 10.5 s, a pause for 10.5 s, and then withdrawal of 20 ml in 10.5 s. This series was repeated 4 times within a block. By infusing more than was withdrawn we repeatedly evoked and abolished sensation without accommodation. Because responses to changes of bladder volume and sensation may differ, we performed measurements at a target volume of 100 ml (2 blocks, evoking little sensation), and again after filling the bladder at 60 ml/min to strong desire to void (2 to 4 blocks, evoking strong sensation).

The functional images were reoriented into standard stereotactic space and the responses relative to rest were calculated using standard statistical procedures (SPM2, Wellcome Department of Imaging Neuroscience, UK). Activity during infusion, post infusion, and during withdrawal was compared with rest.

Results

8 subjects (7 females and one male, aged 23-83 y) were successfully examined. Claustrophobia and technical problems curtailed measurement in 2 other cases. 5 subjects showed detrusor overactivity, 2 of them during the scanning session. 3 subjects showed no detrusor overactivity and had no symptoms suggestive of it.

Activation during and following infusion was demonstrated in the frontal cortex (see figure), the anterior cingulate gyrus, the insula, and the cerebellum in 2 to 5 subjects ($P < 0.05$, corrected for multiple comparisons over the whole brain). Group analysis indicated both cortical and infra-cortical regions of common activation ($P<0.05$), and suggested a trend

towards a different pattern of activation in the subjects with detrusor overactivity (P=0.08). These results will become firmer as this ongoing project accrues subjects.

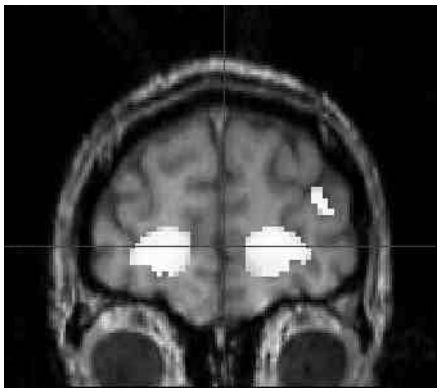

Figure: Bilateral activation in frontal cortex during bladder filling (relative to rest): combined result in 5 subjects. Light areas show significant activations (P<0.05, corrected for multiple comparisons).

Conclusions

Combination of brain fMRI with simultaneous cystometry is physiologically revealing and technically feasible. Responses to bladder filling in cerebellum, insula, and premotor cortex confirm previous reports. Bilateral activation in the frontal cortex may represent inhibition of voiding in response to bladder filling, consistent with clinical observation of the inhibitory role of this region. A different pattern of brain activity in subjects with detrusor overactivity is suggestive of altered cerebral processing that may reflect poor bladder control.