A Preliminary Report on the Use of Functional Magnetic Resonance Imaging with Simultaneous Urodynamics to Record Brain Activity During Micturition

Jan Krhut, Jaroslav Tintera, Petr Holý, Roman Zachoval and Peter Zvara*

From the Department of Urology, University Hospital (JK), Ostrava and Institut of Clinical and Experimental Medicine (JT) and Department of Urology, Thomayer Teaching Hospital (PH, RZ), Prague, Czech Republic, and Division of Urology, Department of Surgery, University of Vermont (PZ), Burlington, Vermont

Abbreviations and Acronyms

fMRI = functional magnetic resonance imaging

MNI = Montreal Neurological Institute

PET = positron emission tomography

Submitted for publication December 2, 2011.

Study received approval from the institutional review board of Thomayer Teaching Hospital, Prague.

* Correspondence: Division of Urology, Department of Surgery, University of Vermont, D319 Given Building, 89 Beaumont Ave., Burlington, Vermont 05405 (e-mail: peter.zvara@uvm.edu).

For another article on a related topic see page 661.

Purpose: We mapped brain activity during micturition using functional magnetic resonance imaging with simultaneous recording of urodynamic properties during slow bladder filling and micturition.

Materials and Methods: We evaluated 12 healthy female volunteers 20 to 68 years old. Eight subjects could urinate while supine. Meaningful data were obtained on 6 of these subjects. Brain activity was recorded continuously during bladder filling and micturition. Functional magnetic resonance imaging measurements made during the micturition phase were used for the final analysis.

Results: Using group statistics we identified clusters of brain activity in the parahippocampal gyrus, anterior cingulate gyrus, inferior temporal gyrus and inferior frontal gyrus during micturition. At the individual level we also observed activation in the upper pontine region, thalamus and posterior cingulum. In subjects unable to void brain activation was documented in the frontal lobe and posterior cingulate gyrus but not in the pons, thalamus or anterior cingulate gyrus. In 5 subjects we identified a relevant pattern of brain activity during the terminal portion of the filling phase when the patient reported a strong desire to urinate.

Conclusions: This new protocol allows for the localization of brain structures that are active during micturition. Data suggest that additional validation studies are needed. Future studies will test modifications that include more detailed monitoring of bladder sensation, stratifying subjects based on age and gender, and increasing the number of data points by adding subjects and the number of micturitions recorded in a single subject.

Key Words: urinary bladder, urination, brain, magnetic brain imaging, neurons

THE last 3 decades have seen great advances in research in the fields of neurourology and neuroregulation of the lower urinary tract. Results from experimental animal models and clinical observations identified 4 main levels of brain control of the lower urinary tract, including the cortex, hypothalamus, midbrain and pons.[1] The development of functional brain imaging using $H_2^{15}O$ PET and fMRI have helped refine these anatomical landmarks.[2–4] The use of fMRI to elucidate central neuroregulation of various organs and systems has grown enormously during the last decade but only a few original research studies have focused on brain control of bladder function using this approach.[5–8]

The activity of neurons in a particular brain region causes a local increase

0022-5347/12/1882-0474/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2012.04.004
Vol. 188, 474-479, August 2012
Printed in U.S.A.

in regional cerebral blood flow, indicating local inhibition or activation of neuronal activity. PET measures this increase based on the distribution of ^{15}O radiolabeled water, which is given by bolus injection in the bloodstream. Due to the short half-life and physical decay of the isotope $H_2^{15}O$ PET only records neuronal activity during a short period. Also, since this technique exposes subjects to significant ionizing radiation, only a single event can be recorded.

fMRI quantifies paramagnetic properties of oxygenated and deoxygenated hemoglobin, which correlate with neuronal activity related changes in blood flow.[9,10] Unlike PET, fMRI does not expose the patient to ionizing radiation and, thus, there are no limitations on recording duration. However, fMRI is characterized by a low signal-to-noise ratio, although it was proposed that objective results can be obtained by averaging many repetitions of a short basic pattern.[11]

fMRI studies of bladder function performed to date have focused on brain activity during the storage phase.[5,12] We used fMRI combined with standard cystometry to map the brain regions that are reproducibly activated during voiding. To control for noise we selected components that correlated with changes in detrusor pressure associated with urination and constructed a map of activated regions common to all subjects. Second level group analysis was then done to determine the topographic site of these activation clusters.

MATERIALS AND METHODS

Subjects

This study was approved by the institutional review board of Thomayer Teaching Hospital, Prague. A total of 12 adult female volunteers 20 to 68 years old (mean ± SD age 49.6 ± 17.0) were recruited. Before study inclusion uroflowmetry was done and post-void residual measurements were made in all subjects. Only those with normal urinary flow and post-void residual less than 10% of functional bladder capacity were included in analysis. Study exclusion criteria were current urinary tract infection, neurogenic bladder, dementia, cystolithiasis, history of pelvic tumor or pelvic radiotherapy, or any technical/medical contraindication to scanning. Before enrollment all subjects read and signed a consent form.

Study Design

A double lumen, soft 6Fr bladder catheter was used for repeat bladder filling and intravesical pressure measurement. Before initiating filling a 10-minute rest period was observed. A rectal catheter was used to measure intra-abdominal pressure. fMRI study was done with the subjects supine using a fixation apparatus to secure the head. Absorbent pads placed under the pelvis allowed subjects to void freely. A handheld signaling device was used to allow subjects to communicate with the examiner.

A bladder catheter was connected to urodynamics equipment positioned outside the magnet room and standard cystometry was done. The bladder was filled with sterile, room temperature 0.9% saline solution at an infusion rate of 50 ml per minute. When a strong desire to void was reported, the subject was prompted to urinate. fMRI continuously recorded brain activity during subsequent micturitions (fig. 1). fMRI data were acquired with a

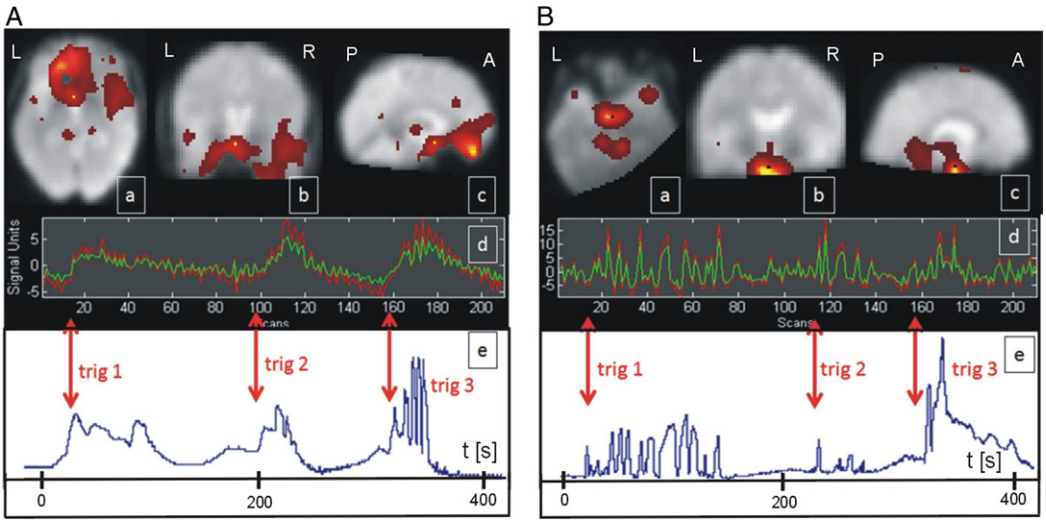

Figure 1. Continuous recording of fMRI brain activity during subsequent micturition cycles shows example of select component of independent component analysis in 2 subjects (*A* and *B*, respectively). Note brain activation main clusters in axial (*a*), coronal (*b*) and sagittal (*c*) planes. Choice of component for analysis was based on good correlation of signal time course (*d*) with bladder pressure changes (*e*) and on patient reported strong desire to urinate (*trig*). Color map represents Z scores with threshold >1. Red curve indicates signal time course maximum in Z score component (*d*). Green curve indicates signal time course maximum in current voxel (left bright dot and right dark dot) (*d*). *t [s]*, time in seconds.