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NEURAL CORRELATES OF VOIDING IN HUMAN SUBJECTS VIA CONCURRENT FUNCTIONAL MAGNETIC RESONANCE IMAGING AND URODYNAMICS

Hypothesis / aims of study

The lower urinary tract has two functions: storage and voluntary elimination of urine. Normal voiding in neurologically intact patients is triggered by the release of tonic inhibition from suprapontine centers, allowing the pontine micturition center to trigger the voiding reflex. Well known animal studies in the literature demonstrate the coordination of spinal centers for bladder function. However, *supra*spinal mechanisms of voluntary storage and voiding in humans is just beginning to be described via functional neuroimaging. In this preliminary study, we seek to discover brain activity processes during voiding via functional magnetic resonance imaging (fMRI) in normal female subjects.

Study design, materials and methods

Ten healthy, premenopausal female volunteers were screened with baseline clinic urodynamics to document normal voiding parameters. We then studied subjects with fMRI and simultaneous urodynamics testing, including the pressure-flow voiding phase. After motion correction, the Generalized Linear Model (GLM) was employed to create individual fMRI activation maps at initiation of voiding. A high-resolution structural scan of the brain was also acquired for transformation of the individual fMRI activation maps into Talairach space. From these transformed datasets, an average fMRI activation map was created, from which areas of significant activation were identified. A preliminary correlation-interaction network analysis was performed of voxels exceeding a threshold of 60% of the largest activation. The correlation coefficient between voxel-intensity time courses served as edge weights. The Molecular Complex Detection (MCODE) clustering algorithm was used to identify brain voxels belonging to each cluster. Transformation back into anatomical space revealed focal and long-range clusters according to fMRI activation established with the GLM model.

Results

Eight of the ten patients were able to void during fMRI scanning. Group analysis of those eight patients yielded consistent areas of activation during the initiation of voiding (asterisks, Figure 1). These included regions for sensorimotor control (cerebellum, thalamus, caudate, lentiform nucleus, red nucleus, supplementary motor area, postcentral gyrus), limbic system (anterior and posterior cingulate gyrus and insula), executive function (left superior frontal gyrus), as well as the parahippocampal gyrus, precuneus, cuneus, occipital lobe (visual system) and a focal region in the midbrain. Preliminary correlation-interaction network analysis of 5 representative subjects were performed with the voxel-intensity time courses for a subject depicted (Figure 2A). This yielded spring-embedded network layouts that for each subject exhibited a small-world structure of focal clusters with short-range interactions connected by long-range edges (Figure 2B). A 3-D representation of cluster connectivity (Figure 2C) showed various clusters in the cerebellum connected to clusters in parietal, frontal and temporal lobes and to clusters in the limbic system mainly via the medial posterior brain regions (e.g. posterior cingulate).

Interpretation of results

By utilizing simultaneous urodynamics, we were able to define and analyze the initiation of voiding as a temporally distinct entity from other time points. At initiation of voiding, structures were activated in sensorimotor and executive areas coordinating the voiding phase. The group analysis also yielded the activation of a focal region in the midbrain which may be the region of the periaqueductal gray and/or the pontine micturition center. In addition, activation of the limbic system (cingulate gyrus and insula), known to occur during bladder filling, reflected both the sensation of fullness and/or discomfort at the time of voiding, as well as a baseline level of anxiety. Network analysis demonstrated the interconnection between these activated brain regions at initiation of voiding.

Concluding message

Our preliminary group and network analyses demonstrate the activation of a brain network consisting of regions for sensorimotor control, executive function, emotion processing, as well as deeper brain structures (midbrain) during micturition. Future investigation will be directed at creating and validating a model of brain activity during normal voiding in women.

Figure 1

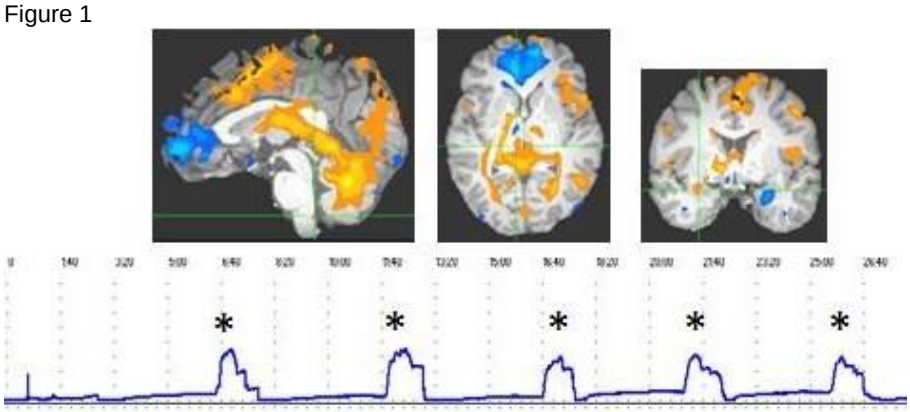

Figure 2

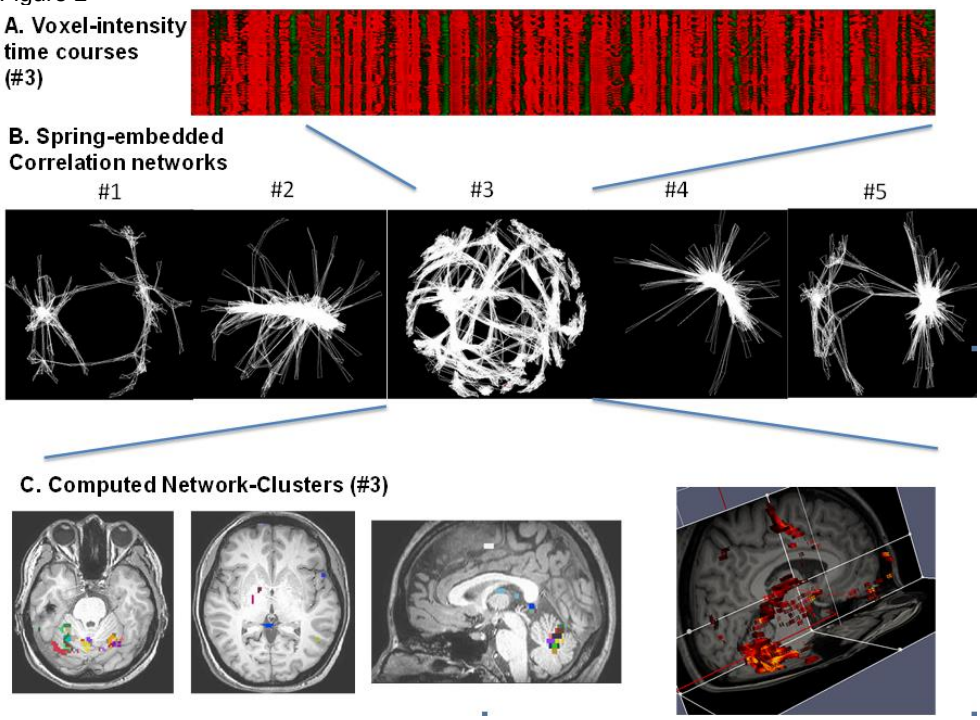

Figure captions:

Figure 1: fMRI activation map after group analysis of patients at initiation of voiding (asterisks)

Figure 2: A: Voxel-intensity time course for subject #3 (Green: elevated signal intensities coinciding with times of voiding). B: Spring-embedded layouts of correlation-interaction networks for five subjects. For each, a small-world structure of focal clusters connected by long-range edges can be appreciated. C: Network clusters for subject #3: clusters in pseudo-color representation displayed in the original anatomical space (left) and displayed in a three-dimensional view (right). Various clusters in the cerebellum show connectivity with parietal, frontal and temporal regions as well as the limbic system mainly via medial posterior structures such as the posterior cingulate.

Disclosures

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