69

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FUNCTIONAL BRAIN ACTIVITY AND WHITE MATTER STRUCTURE ARE IMPAIRED IN ELDERLY URGE-INCONTINENT SUBJECTS COMPARED TO NORMAL CONTROL.

Hypothesis / aims of study

To investigate differences in functional brain activity and structural changes in the white matter between subjects with urgency incontinence and normal control.

Study design, materials and methods

We studied a group of functional community-dwelling older women with urgency incontinence (n=41, average age 72 years) and a group of control subjects without bladder problems (n=13, average age 65 years). Brain activity was assessed using method that combines fMRI with simultaneous urodynamic monitoring in a session consisting of repeated cycles of bladder filling/emptying. We analized functional brain acitivity, in both groups, during blocks of time when subjects reported strong sensation (either urgency or strong desire to void in normals). We used computerized method ('automated labelled pathway') to process structural changes in white matter known as white matter hyperintensities (WMH). We expressed the extent of WMH as a ratio of their total volume divided ('normalized') by each individuals total brain volume to account for individial variations in brain size. We used diffusion tensor imaging (DTI) method to assess fractional anisotropy (FA) in white matter tracts as another measure of structural changes. We also used tract-based spatial statistics method (TBSS) to assess and localize differences in fractional anisotropy as a measure of structural integrity of white matter pathways.

Results

Compared to normal control, subjects with urgency incontinence exhibited greater brain *activations* during urgency, especially in the primary motor cortex and supplemental motor area (SMA) **(Figure 1. Top, left and right)**. In addition, they showed significant *deactivations* in areas of medial prefrontal cortex **(Figure 1. Top, right)**, which were not present in normals. They also had greater global burden of white matter hyperintensities (0.00219 vs. 0.00069, p=0.08). Although there was no difference in global fractional anisotropy readings (0.375 vs. 0.373, p= 0.62) TBSS showed differences in anisotropy in several tracts leading to the regions with significant functional activity (either activated or deactivated) in incontinent subjects **(Figure 1. Bottom, left and right)**.

Interpretation of results

The pattern of brain *activations* of motor areas in both groups is similar but greater in urge-incontinent subjects suggesting increased activity in areas related to urethral sphincter and pelvic floor muscles in order to compensate failure to control the bladder. The *deactivations* in medial prefrontal cortex in incontinent subjects are significant since this area has been shown to activate during voiding in normal volunteers. Since such deactivations do not occur in normal subjects this pattern of activity may represent an imaging marker of functional impairment of central bladder control. Nevertheless, it is imposible to disentagle if such activity represents a cause or consequence of failed control. Possible cause for such change in brain activity may lay in the damaged white matter pathways that connect these functionally relevant areas. Indeed, results of the structural brain imaging studies suggest an increased damage of white matter in urge incontinent subjects and reduced FA in locations/tracts leading to medial prefrontal cortex and other relevant areas.

Concluding message

This is a first study to clearly show diffences in brain function and structure between normal and urge-incontinent elderly subjects. Patterns and locations of such differences are related to medial prefrontal cortex, an executive center involved in control of voiding, and its connecting white matter pathways.

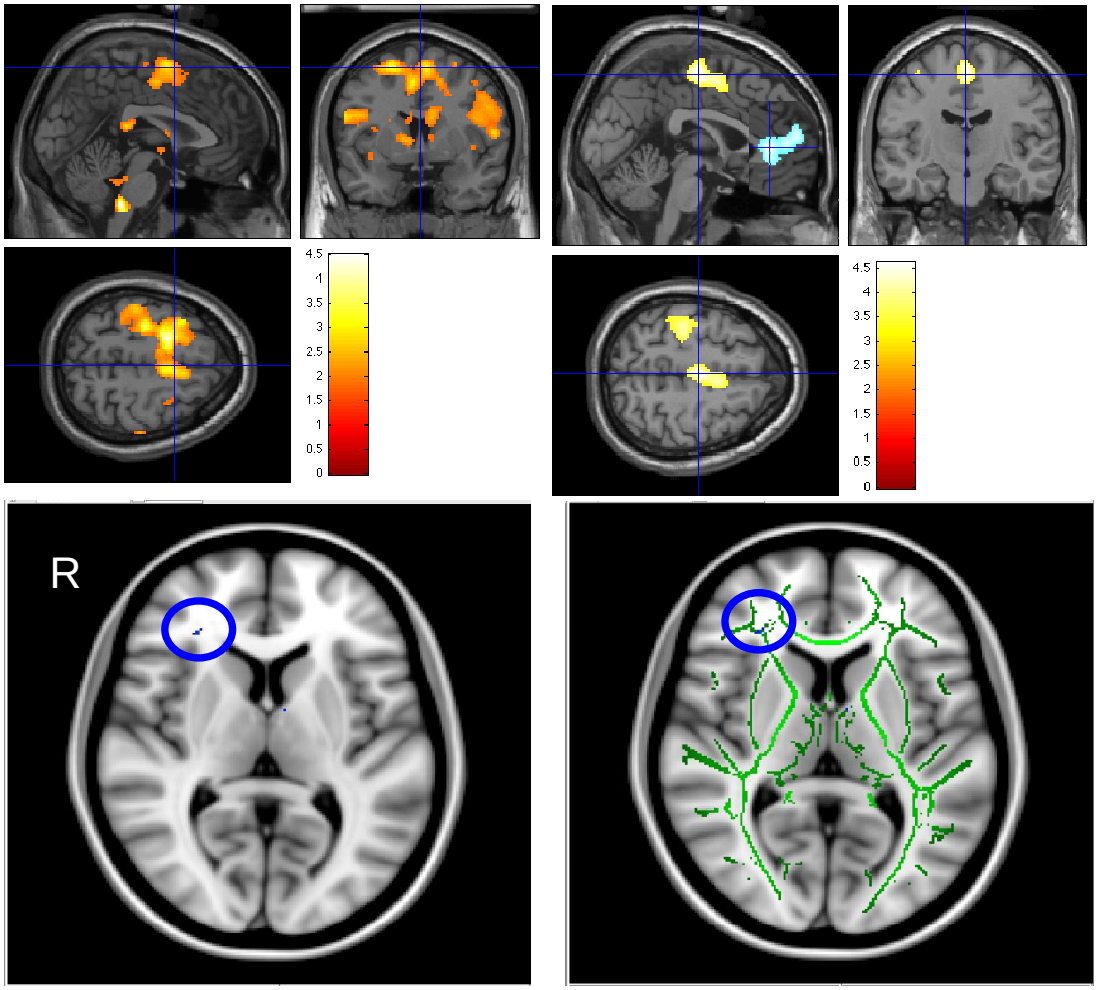

Figure 1 (top): brain activity during bladder filling and reported strong sensation (desire to void or urgency) in normal subjects (**top, left**) and subjects with urgency incontinence (**top, right**). Activated areas in the brain (red-yellow color); deactivated areas (blue color).

Figure 1 (bottom): differences in white matter structure between normal and urge –incontinent subjects. Blue color area (encircled) represents the location of reduced FA in urge-incontinent subjects compared to normal. Green color: white matter tracts ('skeleton').

Disclosures
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