NeuroImage 43 (2008) 183–191

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Gender differences in voluntary micturition control — An fMRI study

S. Seseke [a,*,1], J. Baudewig [b,1], K. Kallenberg [b], R.-H. Ringert [a], F. Seseke [c], P. Dechent [b]

[a] Department of Urology, Georg-August-University, 37099 Göttingen, Germany
[b] MR-Research in Neurology and Psychiatry, Georg-August-University, 37099 Göttingen, Germany
[c] Department of Urology, Martha-Maria Hospital, 06120 Halle, Germany

ARTICLE INFO

Article history:
Received 18 October 2007
Revised 16 July 2008
Accepted 20 July 2008
Available online 5 August 2008

Keywords:
Functional magnetic resonance imaging
Human brain
Micturition control
Pontine micturition centre
Periaqueductal grey
Urge to void
Gender differences

ABSTRACT

In the last decade functional imaging has gained substantial importance for identifying cortical and subcortical brain regions being involved in the micturition circuit. However, possible gender differences are still a matter of debate. In the present study we used functional magnetic resonance imaging (fMRI) to determine micturition related brain regions in healthy men and compared them with those in women to elucidate gender-related differences. fMRI was performed at 3 T in 12 healthy men with urge to void due to a filled bladder. In a non-voiding model they were instructed to contract or to relax the pelvic floor muscles repetitively. As previously reported in women, contraction and relaxation of pelvic floor muscles induced strong activations in the brainstem and more rostral areas in our group of healthy men. In general, men had stronger activations during contraction than women in nearly all identified areas. In contrast, results for the relaxation condition were similar. Some of the differences between contraction and relaxation, formerly detected in females, could be found in our group of males as well. The results suggest that in women and men the same cortical and subcortical networks exist for micturition control. Especially, the well located activations in the putative pontine micturition centre and the periaqueductal grey could be identified in both sexes. However, pelvic floor muscle control seems to induce different activation intensities in men and women.

Introduction

The bladder has two simple functions — storage of urine and its periodic expulsion. These modes of operation are organized in complex circuits. Early research, based on animal and clinical studies, identified the brain structures involved in micturition control. The two central structures serving as relay centres between afferent and efferent pathways are the periaqueductal grey (PAG) as well as the continence and micturition centre in the pons (PMC) (Blok et al., 1995). Both regions are connected with multiple higher centres such as cerebellum, basal ganglia, thalamus, limbic system, insula, and the primary and secondary motor cortices. These higher centres play an important role in modulating the micturition reflex even though they are not responsible for the reflex itself.

In the last decade progress in imaging technologies resulted in several tools like positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) for studying changes in human brain activity. Regarding micturition control increased activity in different cortical and subcortical structures could be elucidated.

The involvement of motor areas, especially the supplementary motor area (SMA) (Di Gangi Herms et al., 2006; Kuhtz-Buschbeck et al., 2007; Seseke et al., 2006; Zhang et al., 2005) and sensory-motor cortex (Blok et al., 1997b; Di Gangi Herms et al., 2006; Seseke et al., 2006), but also parts of the parietal cortex could be found. However, there is still controversy concerning the involvement of the sensory-motor cortex (Athwal et al., 2001; Blok et al., 1997b; Di Gangi Herms et al., 2006; Seseke et al., 2006; Zhang et al., 2005). Furthermore, cortical areas like the insula (Matsuura et al., 2002; Nour et al., 2000) and parts of the prefrontal and parietal cortex have been found activated during pelvic floor muscles contraction or relaxation tasks (Di Gangi Herms et al., 2006; Griffiths et al., 2005; Kuhtz-Buschbeck et al., 2005; Seseke et al., 2006; Zhang et al., 2005). Subcortical activation has been detected in the thalamus (Griffiths et al., 2005; Kuhtz-Buschbeck et al., 2005; Matsuura et al., 2002; Seseke et al., 2006), the basal ganglia (Matsuura et al., 2002; Nour et al., 2000; Seseke et al., 2006; Zhang et al., 2005) and cingulate gyrus (Athwal et al., 2001; Kuhtz-Buschbeck et al., 2005; Kuhtz-Buschbeck et al., 2007; Nour et al., 2000; Seseke et al., 2006; Zhang et al., 2005). Consistently, the cerebellum was found activated in micturition related studies (Athwal et al., 2001; Di Gangi Herms et al., 2006; Griffiths et al., 2005; Kuhtz-Buschbeck et al., 2005; Nour et al., 2000; Seseke et al., 2006; Zhang et al., 2005). The visualization of the two central brainstem structures regulating the micturition and urine withholding, the PMC and PAG, has challenged the functional imaging methods. The PAG could be detected in PET (Athwal et al., 2001; Blok

* Corresponding author. Department of Urology, Georg-August-University, Robert-Koch-Strasse 40, 37075 Göttingen, Germany. Fax: +49 551 396165.
E-mail address: srebman@gwdg.de (S. Seseke).
[1] Equal contribution.

1053-8119/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2008.07.044

et al., 1997a; Blok et al., 1998; Matsuura et al., 2002) as well as fMRI (Griffiths et al., 2005; Kuhtz-Buschbeck et al., 2005; Seseke et al., 2006) studies. While the PMC could be identified in PET studies (Athwal et al., 2001; Blok et al., 1998; Blok 2002; Blok et al., 1997a; Matsuura et al., 2002) in tasks related to micturition and continence control, only a few fMRI studies (Griffiths et al., 2005; Seseke et al., 2006) found it activated.

There is no consensus about gender differences in central micturition control. In an fMRI study comparing differences in activation sites in males and females no gender differences could be found (Kuhtz-Buschbeck et al., 2007). Blok et al. used PET to compare the micturition and continence related activation sites in men and women (Blok et al., 1998). They reported the same recruited sites (pons, cortex, PAG, hypothalamus, cingulate cortex) in both groups with differences in the activation level in the PAG, hypothalamus and insula.

Clinical data regarding gender differences in urinary disorders are controversial. Castro et al. as well as Milsom et al. emphasized, that urinary urgency is more prevalent in women than in men (Castro et al., 2005; Milsom et al., 2000) whereas Stewart et al. interviewed over 5000 adults representative of the US population by age, sex and geographical region with the result, that the overall prevalence of overactive bladder was similar between men (16%) and women (17%) (Stewart et al., 2003).

As shown in perception of emotion (Hofer et al., 2006) or performance of verbal and visospatial tasks (Li et al., 2004) it may be possible that men and women recruit different neural networks or show different levels of activation during micturition or urine withholding. This could be caused by the different genitourinary system anatomies in men and women as well as the different micturition habits. The presence of the prostate and the longer male urethra might have an influence on activated sites and activation level. Furthermore van Haarst et al. (2004) and others (Burgio et al., 1991; Mueller et al., 2005) used urinary diaries to analyze gender differences in urinary habits. They showed that women had lower functional bladder capacities and female voiding frequency was higher than that of males.

In the present study we compared our recently published data on voluntary pelvic floor muscle control in healthy women (Seseke et al., 2006) with a group of healthy men. The aim was first to characterise the network involved in micturition control in men and second to investigate possible gender differences concerning micturition control in activation sites and level in both sexes as these differences have been previously seen in studies focusing on urine withholding and micturition (Blok et al., 1998) and rectal distension as comparable visceral sensation (Kern et al., 2004).

Materials and methods

Subjects

Twelve healthy male adults (mean age ± SD: 32.4 ± 7.9 years, age range 19–49 years) without any history of neurological or psychiatric disease participated in the study. The protocol was approved by the Ethical Committee of the University of Göttingen. All subjects were included after written informed consent. As all the subjects are working in the department of urology they are familiar with the anatomy and function of pelvic floor muscles. Nevertheless, the pelvic floor exercise was explained before the fMRI examination to familiarize every participant with the task.

MR imaging

MR imaging was performed at 3 T (Siemens Magnetom Trio, Erlangen, Germany) using the standard 8-channel phased-array head coil. Subjects wearing headphones for noise protection were placed supine inside the magnet bore. Vital functions were monitored throughout the experiment. Initially, an anatomical T1-weighted MR dataset covering the whole head at 1 mm^3 isotropic resolution was acquired (3D Turbo FLASH, repetition time (TR): 1950 ms, inversion time: 1100 ms, echo time (TE): 3.93 ms, flip angle: 12°). Functional imaging was performed using a T2*-sensitive gradient-echo EPI technique with an in-plane resolution of 2×2 mm^2 (TR: 2000 ms, TE: 36 ms, flip angle: 70°, acquisition matrix: 84×128). Twenty two sections of 4 mm thickness angulated in an axial-to-coronal orientation, covering the whole brain and brainstem structures, including the pons, were acquired. This resulted in high quality single fMRI time series with special emphasis on the brainstem, as shown previously (Seseke et al., 2006).

Paradigm

The subjects were instructed not to void and to drink properly at least 3 h prior to the examination. Furthermore, they were told to report to the MR facility as soon as they sensed a strong desire to void due to a filled bladder. After notification, the fMRI examination started within 30 min. During the functional experiments, the subjects had either to release pelvic floor muscles to mimic the initiation of micturition (RELAX) or to contract pelvic floor muscles to mimic voluntary interruption of the micturition process (CONTRACT). Commands were presented visually using a set of MR-suited LCD glasses (Resonance Technology, Northridge, USA). In an event-related manner, the instructions RELAX and CONTRACT were alternated (2 s each), each followed by a control condition (18 s) during which the subjects had to lie inside the scanner waiting for the next instruction. Consequently, a single cycle of RELAX and CONTRACT with respective control conditions lasted 40 s. Following an initial control period (20 s), each instruction was given 15 times resulting in a total time of 620 s for the fMRI experiment. After the investigation, the participants were asked about proper task execution which was confirmed by every single subject.

Analysis

Functional data were analyzed and visualized using Brain Voyager QX (Brain Innovation, Maastricht, The Netherlands). Preprocessing included 3D motion correction, slice scan time correction, spatial smoothing with a Gaussian kernel (full width at half maximum 8×8×8 mm^3), and linear trend removal. Subsequently, functional datasets were co-registered to the anatomical dataset and transformed into Talairach space. Group analysis was performed using the multi-subject approach of the general linear model. In a first step, the main effects of conditions RELAX and CONTRACT, representing the 2 s-periods of relaxation and contraction of pelvic floor muscles, respectively, convolved with the expected hemodynamic response function, were calculated and the conjunction of both conditions using the random effects model was constructed. In a second step, differential effects (RELAX>CONTRACT and CONTRACT>RELAX) were calculated using the fixed effects model. Finally, both steps were repeated using the male and the female (n = 11) data acquired previously (Seseke et al., 2006) together in one model. The obtained p-values were corrected for multiple comparisons using the false discovery rate approach described previously (Genovese et al., 2002), employing FDR (q)<0,01 and FDR (q)<0,05 for the random and fixed effects analysis, respectively. A cluster size threshold was not used.

Results

Male volunteers

Even though we implemented a non-voiding model, both events (RELAX and CONTRACT) induced strong, well located activations in the pons and PAG in our subjects (Fig. 1). Furthermore, we found activations in the cerebellum, thalamus and putamen, sensory-motor cortex, SMA, parietal cortex, insula and cingulate cortex. The commonly activated regions are listed in Table 1, presenting the group results of the conjunction analysis in a random effects model.