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BRAIN RESPONSES DURING THE URGE TO VOID IN NORMAL MALE VOLUNTEER: A POSITRON EMISSION TOMOGRAPHY STUDY

Hypothesis / aims of study

Recently the number of overactive bladder (OAB) patients increased. The etiology of the urgency is still unclear. To elucidate the association of brain response and urgency or voiding, positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies were performed by several investigators. However, most studies focused on the micturition and maximum desire to void (MDV). First desire to void (FDV) is also important to compare with the urgency. To our knowledge, there are no studies concentrate on the FDV.

To study the association of brain activity and the urge to void or urgency, investigators usually inserted the catheter to fill the bladder with water. The urethral catheter might lead to the uncomfortable sensation which might affect the response of normal desire to void.

In this study, to investigate the human brain mechanism that is activated with the urge to void, we performed a PET study in normal healthy male volunteers without inserting the catheter.

Study design, materials and methods

Six right-handed male healthy volunteers, aged 27-40 years, agreed to participate in this study. The protocol of this study was approved by the local ethical committee. Volunteers drank at least 2 L of water two hours before the study. After volunteers felt maximum desire to void, they were placed in the spine position on the PET scanning bed. A urinary volume monitoring unit (Takeshiba, Kanagawa, Japan) which calculates the urine volume using ultrasonography was worn in the lower abdomen and a self–adhesive external condom catheter was attached to his penis to void the urine. PET scanning was performed with a Headtome V scanner (Shimadzu, Kyoto, Japan). Scans were carried out under the following three conditions: FDV, MDV, post voided status with no sensation of urge to void (POST) (See figure 1). The subjects underwent six to nine sequential regional cerebral blood flow (rCBF) measurements (each condition twice or three times) after a slow i.v. bolus injection of $H_2{}^{15}O$ (259 MBq/scan). The attenuation-corrected data were reconstructed into 3 -dimensional images including the entire cerebrum and cerebellum. The images were realigned by using the first image as a reference, transformed into standard stereotactic space of Montreal Neurological Institute (MNI) and smoothed with an isotropic 12-mm full-width half-maximum Gaussian kernel by statistical parametric mapping software (SPM2) (Wellcome Department of Cognitive Neurology, London, UK). PET images of the FDV and MDV conditions were then statistically compared with those of the POST condition on a voxel-by-voxel basis. An uncorrected *P*-value less than 0.001 were considered significant in this study.

Results

FDV (FDV minus POST) was associated with the increased blood flow in the bilateral cerebellum, right parahippocampal gyrus, left superior frontal gyrus and left cingulate gyrus. Decreased blood flow (POST minus FDV) was found in the right superior temporal gyrus, right uncus, right cingulate gyrus, left middle temporal gyrus and left medial frontal gyrus.

MDV (MDV minus POST) was associated with increased blood flow in the bilateral cerebellum, left inferior frontal gyrus, left globus pallidus, right insula, left midbrain, left thalamus. Decreased blood flow (POST minus MDV) was found in the bilateral uncus, bilateral occipital gyri, bilateral temporal gyri, bilateral frontal gyri, left postcentral gyrus, right anterior cingulated, right superior parietal lobule and right precuneus

Interpretation of results

Brain activity in the MDV condition could include the strong desire to void, the inhibition of micturition and pelvic floor contraction. As similar as the previous PET and fMRI studies, blood flow in various brain regions including insula, midbrain, frontal gyrus and cerebellum increased and also blood flow in various regions decreased.

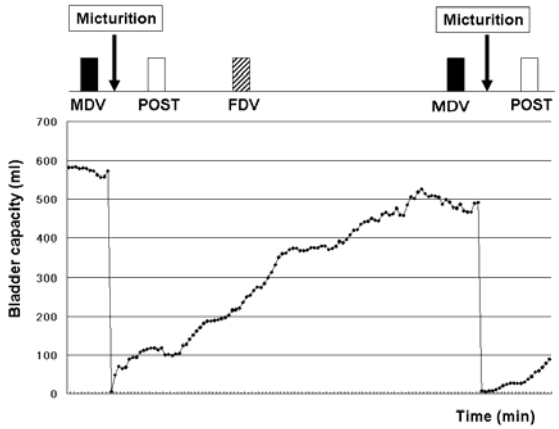
In FDV, the increased blood flow was only found in the bilateral cerebellum, right parahippocampal gyrus, left superior frontal gyrus and left cingulate gyrus. Previous report showed the cerebellar activation is thought to be brought by activation of c-fibers. Other reports showed the association of non-painful bladder distension and c fiber-mediated component in rat studies. The cerebellum could be associated with FDV. Other report showed that the activation of cingrate gyrus was correlated with increasing bladder volume. We also showed the activation of cingrate cortex. Previous fMRI study also showed the parahippocampal gyrus was activated in bladder voiding control. This means the limbic system is involved in visceral sensation.

Concluding message

Although trial group are small, we found the brain activity associated with the sensation of FDV and MDV. This urine monitoring system and condom type catheters were less invasive methods than cystometry. The combined activation of bilateral cerebellum, right parahippocampal gyrus, left superior frontal gyrus and left cingulated gyrus could be correlated with the FDV.

Further study performed in the OAB patients might elucidate the urgency to compare with the results found in this study.

Figure 1



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