🏆 **PRIZE AWARD: Best Clinical Abstract (Joint Prize)**

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ABNORMAL BRAIN RESPONSES TO BLADDER FILLING IN YOUNG WOMEN WITH URINARY RETENTION AND EFFECT OF SACRAL NEUROMODULATION

Hypothesis / aims of study

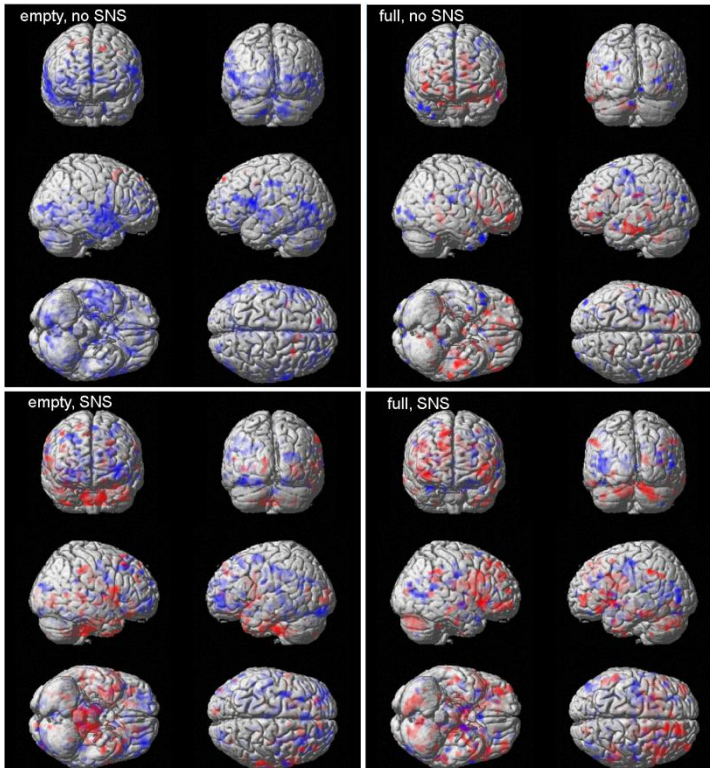
A subset of young women with chronic urinary retention of a particular pathogenesis may have little bladder sensation and be unable to contract the detrusor. In this condition voiding is impaired or impossible and catheterization is usually necessary. The condition is characterized by elevated maximum urethral closure pressure (MUCP) and abnormal EMG recordings from the striated urethral sphincter. Impairment of filling sensation suggests that bladder afferent signals reaching the brain may be weak or absent. Sacral neuromodulation (SNM) does not alter the sphincter abnormality but does restore a degree of bladder sensation and the ability to micturate. The aims of this study were therefore to use functional magnetic resonance imaging (fMRI) of the brain to determine cerebral responses to bladder filling before and after SNM. We hypothesized that altered responses at baseline in the patients may be restored by SNM.

Study design, materials and methods

Six female volunteers aged 18 – 39 y were included, having been referred with urinary retention and a diagnosis made. A 1.5T scanner was used for fMRI pre- and post-SNM. On each occasion two measurement sessions were performed, one with near-empty bladder and the other with the bladder filled until strong desire to void or report of discomfort. After structural imaging, the whole brain was scanned (once per 3.24 s, 280 total scans) to measure regional neuronal activity. During scanning, 50 ml saline was repeatedly infused or withdrawn from the bladder over a period of 7 s, thus mimicking repeated bladder filling. A push-button was used by the patient to report changes in desire to void. Images were preprocessed and analysed using Statistical Parametric Mapping (SPM2). The difference between fMRI signals during infusion and withdrawal was used to indicate response to bladder filling.

Results

Brain responses to bladder infusion and sensation (judged by number of button presses) depended on both bladder volume (near-empty or full) and SNM status (pre- or post-SNM), as shown in the figure. Pre-SNM and with near-empty bladder (top left panel), sensation was weak and responses were almost exclusively negative (deactivation, blue in figure) rather than the normal positive activations. Abnormality of response (deactivation) was correlated with higher MUCP. With full bladder and post-SNM (lower right panel), sensation improved and limited activation (red in figure) was observed in some parts of the cortex. The midbrain periaqueductal grey (PAG), which receives ascending afferents from the spinal cord, showed a similar trend.



Interpretation of results

Brain responses to bladder infusion in subjects with this syndrome are highly abnormal. The extent of the abnormality is correlated with the severity of the condition as represented by urethral pressure, confirming a pathophysiological association between them. After successful SNM treatment, the reliability of bladder sensation is improved and brain responses to bladder infusion are partially normalized. The behaviour of the midbrain PAG, gateway to the higher parts of the brain, is particularly interesting. At baseline and with empty bladder the PAG shares in the general trend to deactivation by bladder filling, suggesting that bladder afferents never reach it. After SNM and with increased bladder volume, the PAG too shows a trend to activation. One possible interpretation is that, in this syndrome, abnormal afferents from an overactive or oversensitive urethral sphincter suppress bladder afferents via a spinal

pro-continence reflex. Consequently the PAG and the rest of the brain receive little input, thus reducing bladder sensation and contractility.

Concluding message

In this condition of urinary retention, an involuntarily overactive sphincter exaggerates the spinal pro-continence reflex. By suppressing bladder afferents, PAG activation is blocked, sensation eliminated and detrusor contraction inhibited. SNM appears to re-open afferent pathways to the brain, thus re-enabling sensation and voiding.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Local Research Ethics Committee, London, UK**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**