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MODULATION OF ANTERIOR CINGULATE, HIPPOCAMPAL, AND PONTINE ACTIVITY ASSOCIATED WITH SACRAL NERVE ROOT STIMULATION THERAPY

Hypothesis / aims of study

Sacral neuromodulation has been successfully utilized in the treatment of voiding dysfunction including symptoms of frequency, urgency, urge incontinence, urinary retention, and painful bladder syndrome. The mechanism of action of sacral neuromodulation remains unknown. The purpose of this study was to examine its effects on the central nervous system.

Study design, materials and methods

Nine subjects were recruited from a Urology clinic after surgical implantation of devices (Medtronic, Inc.) designed to deliver electrical stimulation to sacral nerve roots. Each had eight 2-min PET scans following i.v. administrations of 555MBq[O-15]water. PET data were transformed to MNI template space using SPM2, and examined for significant changes in regional activity across 4 conditions-- device current off, expectation of current (with current actually set to zero), higher current causing detectable sensation, and lower current with no detectable sensation-- with each condition presented twice in a counterbalanced fashion to control for order effects

Results

After statistical correction for multiple regional comparisons, it was found that high-intensity sacral neuromodulation was associated with decreased activity in left dorsal anterior cingulate cortex (ACC), relative to both the 'off' and 'expectation' control conditions ($p<0.0005$ and $p<0.001$, respectively), while no significant modulation of activity in this area occurred during low-intensity stimulation relative to either control condition. Concurrently, high-intensity sacral neuromodulation was associated with increased activity in pons, right hippocampus, and right perigenual ACC relative to the 'off' control ($p<0.002$ for all regions); among these regions, increased activity during low-intensity stimulation persisted in the perigenual area ($p=0.005$).

Interpretation of results

Sacral neuromodulation in patients with urogenital distress syndromes was associated with decreased activity in the dorsal ACC region (linked with perception of painful somatic stimuli), and concurrently increased activity in the perigenual ACC (linked with descending pain inhibitory central mechanisms), as well as in hippocampus and pons.

Concluding message

These findings may point to key brain regions involved in neuromodulation therapy of voiding dysfunction syndromes.

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HUMAN SUBJECTS: This study was approved by the Internal Review Board, UCLA. and followed the Declaration of Helsinki Informed consent was obtained from the patients.