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BRAIN ACTIVATION DURING DETRUSOR OVERACTIVITY IN PATIENTS WITH PARKINSON DISEASE: A POSITRON EMISSION TOMOGRAPHY STUDY

Hypothesis / aims of study

Patients with Parkinson disease (PD) often exhibit storage symptoms such as daytime urinary frequency, urgency, and urinary incontinence, which are induced by detrusor overactivity (DO). However, little is known of the mechanism inducing DO in this disease. We previously examined human brain response to bladder filling in right-handed healthy male volunteers using Positron Emission Tomography (PET) [1]. We hypothesized that brain activation patterns in response to bladder filling would be different in patients with PD. To our knowledge, no PET study has been explored in patients with PD to elucidate the pathophysiology of DO.

Study design, materials and methods

Nine male patients with PD (age 52-76 years, mean age 63 years, all right-handed, mean duration of the disease was 8 years) were examined. The Hoehn and Yahr stage of disability scale in PD was stage 3 in 6 patients and stage 4 in 3 patients. An 8 Fr urethral catheter was introduced and connected to a cystometry device. Patients were placed at spine position in a PET camera (ECAT EXACT HR+, Siemens-CTI, USA). In each case, a scanning session consisting of task 1 (under empty bladder) and task 2 (under DO) was repeated 3 times for a total of 6 scans. For task 1 the bladder was maintained empty by the urethral catheter drainage. For task 2 water at room temperature was dripped for bladder filling and stopped when DO was detected. Before each scan, 300 MBq of $H_2{}^{15}O$ in saline was intravenously injected. Data acquisition was initiated 40 seconds after the beginning of injection and continued for 90 seconds. Intravesical pressure was monitored throughout the procedure. After a task 2 scan the bladder was emptied again for task 1 of the next scan. The data of each scan were summated on a computer and further analyzed using the Statistical Parametric Mapping procedure. A corrected p-value less than 0.05 was considered significant.

Results

During bladder filling, DO was noted in all patients. Mean volume threshold of DO on cystometry was 193 ml (range 80 to 450). Compared with the bladder empty, bladder filling associated with DO (tasks 2 minus 1) significantly activated several brain regions. Significant brain activation during DO was found in the periaqueductal gray, thalamus, cerebellar vermis, putamen, insula, and also in the part of middle frontal gyrus (Brodmann's area 6), called the supplementary motor area (Table 1).

Interpretation of results

Compared with previous results in healthy volunteers, the periaqueductal gray, insula, putamen and thalamus were common activation sites responding to bladder filling. The cerebellar activation in patients with PD was larger than in healthy volunteers. However, the pons was not activated during bladder filling in patients with PD. The alteration in brain activation sites in response to bladder filling seems to be the underlying pathophysiology of DO in patients with PD.

Concluding message

This study, although preliminary, is the first functional neuroimaging studies to investigate DO in patients with PD. Further studies will bring much information regarding cerebral processing of micturition reflex in PD, and enable us more precise understanding of pathophysiology and better treatment strategy for storage symptoms.

Reference

1. Human brain region response to distention or cold stimulation of the bladder: a positron emission tomography study. J Urol 168: 2035-2039

Table 1: Brain regions significantly activated during DO

Brain region	Side	Peak Activation Position(mm.)			Z score
		x	y	z	
Periaqueductal gray	Left	-7	-35	-10	2.33
Thalamus	Right	-8	-22	0	3.75
	Left	8	-16	0	3.69
Cerebellum	Vermis	0	-58	-18	4.99
Putamen	Left	-24	6	14	3.06
Insula	Left	-38	6	6	4.20
Supplementary motor area (Broadmann area 6)	Bilateral	-4	-20	62	3.84

Results of comparisons of DO condition at rest.
Coordinates are given in standard stereotaxic space (Talairach and Tournoux, 1988) in millimetres for the maximally significant pixel in each area in the order x, y, z. X is the lateral displacement from the midline, y is the anterior–posterior displacement relative to the anterior commissure, z is the vertical displacement relative to the anterior–posterior commissure line. Threshold used for display was corrected to $p < 0.05$.