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## URINARY DYSFUNCTION AND RIGHT FRONTAL HYPOPERFUSION IN IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS; AN [<sup>123</sup>I]-IMP SPECT STUDY

### Hypothesis / aims of study

To elucidate the pathophysiology of the urinary dysfunction in idiopathic normal pressure hydrocephalus (iNPH).

### Study design, materials and methods

Urinary symptoms were observed and single-photon emission computed tomography (SPECT) brain imaging performed in 100 patients with clinico-radiologically definite iNPH.<sup>1</sup> They were 58 men, 42 women; mean age, 74 years old (60-84 years). SPECT perfusion imaging was obtained by an injection of 111 MBq of N-isopropyl-p-[<sup>123</sup>I]-iodoamphetamine (IMP), which was immediately trapped and stabilized within the brain. Using NEUROSTAT (3D-SSP) software<sup>2</sup>, statistical difference of normalized mean tracer counts was calculated and visualized between two groups, e.g., patients with urinary dysfunction of severer degrees (grade 2, urinary incontinence 1-3 times a week; 3, urinary incontinence 4-7 times a week; and 4, loss of bladder control) and those of milder degrees (grade 0, none; and 1, urinary frequency or urgency) in iNPH grading scales urinary subscales<sup>1</sup>.

### Results

A) There was a significant decrease in tracer activity in right-side-dominant bilateral frontal cortex and left inferior temporal gyrus as compared to the group of mild urinary dysfunction ( $p < 0.05$ ) (**Figure 1**). In addition, there was a significant increase in tracer activity in right superior frontal gyrus, right medial frontal and parietal gyrus, bilateral posterior cingulate gyrus, and left pontine-mesencephalic area ( $p < 0.05$ ). B) We analyzed a subset of patients in a single gait category (grade 1, mild, subjective walking difficulty alone) among 0-4 grades (larger number indicates severe dysfunction). Among the patients, there was also a significant decrease in tracer activity in right frontal cortex related with urinary dysfunction. Similarly, we analyzed patients in a single cognitive category (grade 1, mild, subjective memory disturbance alone). Among the patients, there was also a significant decrease in tracer activity in right frontal cortex related with urinary dysfunction.

### Interpretation of results

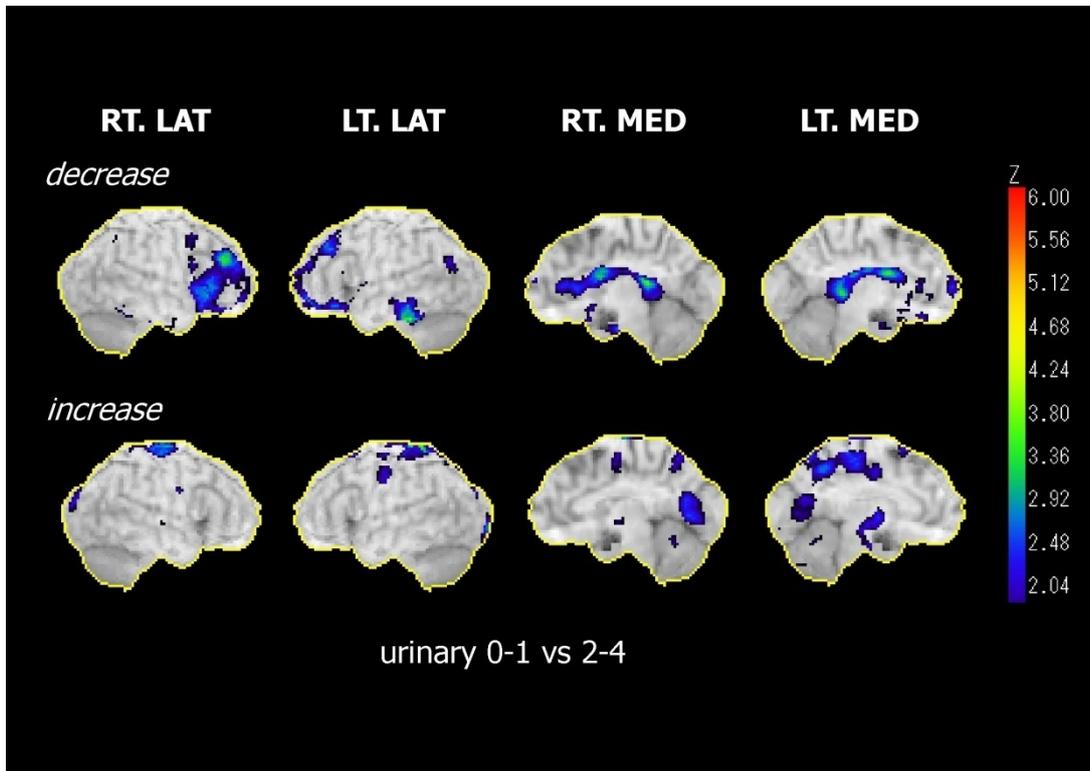
Since iNPH is a diffuse brain disease with dilated ventricles, the site of lesions accounting for urinary dysfunction has remained unclear in this disorder. To the best of our knowledge, this is the first report to show that urinary dysfunction in iNPH is closely related with right frontal hypoperfusion using [<sup>123</sup>I]-IMP SPECT. Previous studies have suggested that the frontal cortex is critical in supra-pontine regulation of micturition reflex. The net effect of the frontal cortex on micturition is thought to be inhibitory, since lesion in this area has led to urinary incontinence in experimental animals and humans. Functional imaging studies in normal volunteers have indicated the predominance of right hemisphere on micturition<sup>3</sup>, which is consistent with the results in the present study. Since right frontal hypoperfusion related with urinary dysfunction was also observed in the subgroup of patients with adjusted gait or cognitive grades, urinary dysfunction in iNPH might occur independently from gait or cognitive disturbance.

### Concluding message

Urinary dysfunction is closely related with right frontal hypoperfusion in iNPH using [<sup>123</sup>I]-IMP SPECT. Not only secondary incontinence due to immobility or dementia, but also neurogenic mechanism might underlie the urinary dysfunction, which is a significant burden in the patients with iNPH and their caregivers.

### References

- 1 Neurol Med Chir (2004) 44: 222-223.
- 2 J Nucl Med (1994) 35: 1528-1537.
- 3 J Comp Neurol (2005) 493: 27-32.



**Figure 1** 3D- SSP maps of differences of cerebral blood flow as measured by [ $^{123}\text{I}$ ]-labelled IMP between two groups, e.g., patients with urinary dysfunction of severer degrees (grade 2, urinary incontinence 1-3 times a week; 3, urinary incontinence 4-7 times a week; and 4, loss of bladder control) and those of milder degrees (grade 0, none; and 1, urinary frequency or urgency) in iNPH grading scales urinary subscales. Upper row: area of decrease in the cerebral blood flow ( $p < 0.05$ ), lower row: area of increase in the cerebral blood flow ( $p < 0.05$ ). Differences just adjacent to the ventricle might be an artefact of the ventricular enlargement. Probability is converted to Z-score.

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**HUMAN SUBJECTS:** This study was approved by the Ethics committee in Chiba University and followed the Declaration of Helsinki Informed consent was obtained from the patients.