Usefulness of the convexity apparent hyperperfusion sign in ^{123}I -iodoamphetamine brain perfusion SPECT for the diagnosis of idiopathic normal pressure hydrocephalus

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OBJECTIVE The gold standard for the diagnosis of idiopathic normal pressure hydrocephalus (iNPH) is the CSF removal test. For elderly patients, however, a less invasive diagnostic method is required. On MRI, high-convexity tightness was reported to be an important finding for the diagnosis of iNPH. On SPECT, patients with iNPH often show hyperperfusion of the high-convexity area. The authors tested 2 hypotheses regarding the SPECT finding: 1) it is relative hyperperfusion reflecting the increased gray matter density of the convexity, and 2) it is useful for the diagnosis of iNPH. The authors termed the SPECT finding the convexity apparent hyperperfusion (CAPPAH) sign.

METHODS Two clinical studies were conducted. In study 1, SPECT was performed for 20 patients suspected of having iNPH, and regional cerebral blood flow (rCBF) of the high-convexity area was examined using quantitative analysis. Clinical differences between patients with the CAPPAH sign (CAP) and those without it (NCAP) were also compared. In study 2, the CAPPAH sign was retrospectively assessed in 30 patients with iNPH and 19 healthy controls using SPECT images and 3D stereotactic surface projection.

RESULTS In study 1, rCBF of the high-convexity area of the CAP group was calculated as 35.2–43.7 ml/min/100 g, which is not higher than normal values of rCBF determined by SPECT. The NCAP group showed lower cognitive function and weaker responses to the removal of CSF than the CAP group. In study 2, the CAPPAH sign was positive only in patients with iNPH (24/30) and not in controls (sensitivity 80%, specificity 100%). The coincidence rate between tight high convexity on MRI and the CAPPAH sign was very high (28/30).

CONCLUSIONS Patients with iNPH showed hyperperfusion of the high-convexity area on SPECT; however, the presence of the CAPPAH sign did not indicate real hyperperfusion of rCBF in the high-convexity area. The authors speculated that patients with iNPH without the CAPPAH sign, despite showing tight high convexity on MRI, might have comorbidities such as Alzheimer's disease.

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KEY WORDS cerebral blood flow; convexity apparent hyperperfusion sign; idiopathic normal pressure hydrocephalus; ^{123}I -IMP SPECT

IDIOPATHIC normal pressure hydrocephalus (iNPH) is characterized by the clinical triad of gait disturbance, cognitive decline, and urinary incontinence in patients with ventricular enlargement and a normal mean intracranial

pressure, occurring without secondary causes of NPH.^{1,5} A precise diagnosis is very important because iNPH is treatable by permanent drainage of CSF. The international guidelines for iNPH recommended CSF tap and CSF drain-

ABBREVIATIONS ^{123}I -IMP = ^{123}I -iodoamphetamine; ARG = autoradiography; CAP = patients with the CAPPAH sign; CAPPAH = convexity apparent hyperperfusion; CBF = cerebral blood flow; DESH = disproportionately enlarged subarachnoid space hydrocephalus; FAB = Frontal Assessment Battery; iNPH = idiopathic normal pressure hydrocephalus; iNPHGS = iNPH Grading Scale; MMSE = Mini-Mental State Examination; NCAP = patients without the CAPPAH sign; rCBF = regional CBF; ROI = region of interest; SEE = stereotactic extraction estimation; SSP = stereotactic surface projection; TMT-A = Trail Making Test A; TUG = Timed Up and Go.

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age tests for diagnosis.^{17,23} The CSF drainage test has been reported to exhibit both high sensitivity and specificity,^{17,30} but it is invasive for elderly patients with symptoms of iNPH as the drain needs to be implanted for several days.

The international guidelines for iNPH do not include any neuroimaging criteria. The Japanese iNPH guidelines, however, indicate that a disproportionately enlarged subarachnoid space hydrocephalus (DESH) sign,^{4,22} which is a characteristic MRI finding of tight high convexity,¹³ and an enlarged Sylvian fissure with ventricular dilation are important for the diagnosis. Two Japanese multicenter prospective studies confirmed the benefit of shunt surgery for patients with iNPH with the DESH sign on MRI without the support of the CSF tap test.^{4,12} Tight high convexity is defined in the Japanese guidelines as the “disappearance of the sulci in two sequential sections on coronal T1-weighted MRI.” However, there are some cases in which it is difficult to judge whether high-convexity tightness is present or absent.

Cerebral blood flow (CBF) images generated by SPECT, which are not measured quantitatively, often show the “hyperperfusion” sign of high-convexity areas in patients with iNPH (Fig. 1). In this study, we determined whether the hyperperfusion sign was apparent or real and whether it was useful for the diagnosis of iNPH. We hypothesized that this finding was an apparent hyperperfusion, not a real one, because of the increased gray matter density in the convexity areas in patients with iNPH.¹⁰ Furthermore, we considered this hyperperfusion to be a highly characteristic sign of iNPH.

We referred to this as the “convexity apparent hyperperfusion” (CAPPAH) sign. The term “CAPPAH” sounds like “Kappa,” which, in Japanese folklore, is a goblin that lives in water and has a plate of water on its head. The apparent hyperperfusion area on the vertex looks like the plate on Kappa’s head (Supplemental Fig. 1).

Methods

We conducted 2 clinical studies. Study 1 was a quantitative regional CBF (rCBF) study to determine whether the CAPPAH sign was apparent or real. Study 2 was a comparative study of patients with iNPH and controls to determine whether the CAPPAH sign was useful for the diagnosis of iNPH. All participants were diagnosed and treated at our institution and provided written informed consent to participate in the study, which was approved by the Ethics Committee of our institution. The study procedures were designed and performed in accordance with the Declaration of Helsinki.

Study 1

Twenty consecutive patients (13 men and 7 women, mean age [$\pm$ SD] 78.2 ± 6.02 years, range 66–89 years), who were diagnosed with “possible iNPH with MRI support,”²² were prospectively enrolled in study 1 from July 2012 to February 2015. Clinical histories were obtained, and physical and neurological examinations were conducted for all participants. Furthermore, we performed CSF tap tests and iNPH evaluation tests that included the Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB), Trail Making Test A (TMT-A), 3-me-

FIG. 1. A representative case with indistinct DESH and distinct CAPPAH signs. Coronal FLAIR MR image (A) and axial and sagittal CBF SPECT images (B) of an 81-year-old woman suffering from gait disturbance and urinary incontinence. In the MR images, the DESH finding is indistinct because the subarachnoid spaces in the high-convexity area are narrow but the sulci can still be seen. In contrast, the CBF SPECT images show distinct hyperperfusion in the high-convexity area (the CAPPAH sign). Axial and sagittal CBF SPECT images (C) of a 69-year-old man with no neurological symptoms or cognitive deficits are also shown.

ter Timed Up and Go (TUG) test, and idiopathic Normal Pressure Hydrocephalus Grading Scale (iNPHGS)¹⁶ before and 7 days after the removal of CSF (30 ml). At CSF removal, routine CSF analyses were performed for all patients. A positive CSF tap test was defined as an improvement of 1 or more points in iNPHGS scores, more than 10% on the TUG test, or 3 or more points on the MMSE at 7 days after CSF removal. All patients underwent ¹²³I-io-damphetamine (¹²³I-IMP) SPECT, which was performed for a differential diagnosis. The details of ¹²³I-IMP SPECT are presented in Supplemental Methods. Visual inspection of CBF SPECT images was performed. On a CBF SPECT image, the CAPPAH sign was determined as positive if it fulfilled the following 2 conditions: 1) on axial slices, the relative CBF of the high-convexity area increased in either a circular pattern (Fig. 2A) or a linear pattern along the superior sagittal sinus (Fig. 2B); and 2) on coronal slices, while the relative CBF of the high-convexity area and the medial parietal lobe increased, the relative CBF

FIG. 2. Definition of the CAPPAH sign using axial and coronal CBF SPECT images in patients with iNPH. In coronal slices, the relative CBF of the high-convexity area and medial parietal lobe is increased. On axial slices, the relative CBF of the high-convexity area is increased in a circular (A) or linear (B) pattern along the superior sagittal sinus.

of the lower parietal and temporal lobes did not increase (Fig. 2). For the interpretation of CBF SPECT images, 2 experienced neurologists familiar with neuroimaging-based diagnosis (T.O. and M.K.), who were blinded to the diagnosis of each participant, judged whether hyperperfusion of the high-convexity area existed. Patients were classified into groups with the CAPPAH sign (CAP) and without the CAPPAH sign (NCAP). The 2 groups were compared regarding scores of the iNPH evaluation tests and responses to the CSF tap test. Furthermore, rCBF in the high-convexity area was examined with rCBF maps using ^{123}I -IMP autoradiography (ARG)⁷ and the stereotactic extraction estimation (SEE)²¹ method. The details of the ARG and SEE methods are presented in Supplemental Methods. “Paracentral lobule,” “superior parietal lobule,” and “precuneus” in Talairach Daemon Level 3²⁸ were defined as the high-convexity area in the study (Fig. 3).

Study 2

Thirty consecutive patients with iNPH (18 men and 12 women, mean age 75.8 ± 5.90 years, range 62–85 years) were retrospectively investigated in study 2 between January 2005 and December 2010. The patients with iNPH examined in this study consisted of those with “probable” ($n = 22$) or “definite” ($n = 8$) iNPH, diagnosed according to the clinical guidelines for iNPH proposed by the Japanese Society of Normal Pressure Hydrocephalus.¹¹ All the iNPH patients examined also satisfied the criteria for “probable” iNPH of the international guidelines for iNPH. At the time of diagnosis, a full clinical history was taken, and physical and neurological examinations, MMSE scores, and routine CSF analyses were performed for all

patients. In addition, 19 age-matched healthy controls (9 men and 10 women, mean age 75.1 ± 7.12 years, range 65–92 years) were enrolled between January 2001 and December 2003. The healthy controls did not show the triad of iNPH, or MRI abnormality. All patients underwent MRI of the brain and ^{123}I -IMP SPECT, which were performed for a differential diagnosis. The obtained data from SPECT images were analyzed with image analysis software (iNEUROSTAT ++, Nihon Medi-Physics Co., Ltd.), developed by Minoshima et al.²⁰ We obtained surface-projected perfusion images plus Z-score (normal mean – individual value/normal SD) maps from the anatomically standardized images. Then, these 3D stereotactic surface projection (3D-SSP) images were used for image interpretation. In our 3D-SSP analyses, a normal database was constructed from the brain perfusion SPECT data of 20 healthy subjects (10 men and 10 women, mean age 72.1 ± 6.2 years). None of these healthy subjects included in the normal database had a history of neurological or psychiatric disorders, cognitive deficits (MMSE score 29–30), or major medical illness. To quantify perfusion differences, the normalized brain activity of each patient was compared with that of the normal database using pixel-by-pixel Z-score analysis. The Z-score maps were displayed with a 2-tailed view, designed to exhibit increased (red to yellow) and decreased (dark blue to light blue) Z-score regions in a schematic brain.²⁵ The usefulness of the CAPPAH sign on CBF SPECT images was compared with that on 3D-SSP images. Visual inspection of CBF SPECT images was performed retrospectively in a similar manner to study 1. On a 3D-SSP image, the CAPPAH sign was determined as positive if the relative CBF

FIG. 3. Three regions regarded as the high-convexity area at the gyrus level. In our study, the 3 areas of the paracentral lobule (green), superior parietal lobule (blue), and precuneus (red), the Talairach Daemon Level 3 regions used in the SEE method, are defined as the high-convexity area.

FIG. 4. Definition of the CAPPAAH sign using 3D-SSP images. On 3D-SSP images in a patient with iNPH, the high-convexity area is represented in red, which means that the relative CBF is increased. CBL = cerebellum as reference regions; GLB = global brain regions as reference regions; INF = inferior view; LT.LAT = left lateral view; LT.MED = left medial view; PNS = pons as reference regions; POST = posterior view; RT.LAT = right lateral view; RT.MED = right medial view; SUP = superior view; THL = thalamus as reference regions.

of the high-convexity area increased equivalent to condition 1 or 2 in study 1 (Fig. 4).

Statistical Analysis

The differences in characteristics, MMSE, FAB, TMT-A, TUG, iNPHGS, and quantified rCBFs between the CAP and NCAP groups in study 1 were analyzed using the Mann-Whitney U-test. Agreement between the 2 neurologists on the assessment of the CAPPAAH sign was analyzed using the κ statistic. The difference in the number of CSF tap responders between the CAP and NCAP groups in study 1 and the differences between the 2 groups in study 2 were analyzed using Fisher's exact test. The minimum level of significance was designated as $p < 0.05$. Statistical analyses were conducted with the GraphPad Prism program (version 6.0, GraphPad Software).

Results

Study 1

Results of CAPPAAH Sign Assessment

Fifteen (75%) of the 20 patients in study 1 were classified as CAP and 5 (25%) as NCAP. Agreement between the 2 neurologists on the assessment of the CAPPAAH sign

was excellent ($\kappa = 0.875$). There was disagreement on the assessment of only 1 case, which was ultimately diagnosed by an expert neuroradiologist. No significant differences between the CAP and NCAP groups were found with regard to age or sex. Clinical and laboratory data in the CAP and NCAP groups in study 1 are summarized in Table 1. Concerning iNPHGS subscores, no significant differences between the CAP and NCAP groups were found (gait [$p > 0.99$], cognitive [$p = 0.25$], and urinary [$p = 0.83$]). As assessed by the TUG test, there were no significant differences in gait speed between the CAP and NCAP groups ($p = 0.246$). On cognitive examination, MMSE scores in the NCAP group were significantly lower than those in the CAP group ($p = 0.043$), but no significant differences were found in FAB scores ($p = 0.127$) or in the tracking performance of the TMT-A ($p = 0.868$). The rate of responses in the CSF tap test was significantly lower in the NCAP group (0%) than in the CAP group (60%; $p = 0.044$). Eight of the 9 responders showed more than a 10% improvement on the TUG test, and the remaining responder showed a 6-point improvement on the MMSE at 7 days after CSF removal. The TUG time in the NCAP group was significantly higher at 7 days after CSF drainage ($p = 0.014$) and showed less of an improvement than that of the CAP group on the CSF tap test ($p = 0.025$; Table 2). For the treatment

TABLE 1. Clinical and laboratory data of the CAP and NCAP groups in study 1

Variable	CAP (n = 15)*	NCAP (n = 5)*	p Value†
Duration from onset (mos)	39 ± 17.4	29.4 ± 19.0	0.257
iNPHGS			
Gait (0–4)	1.8 ± 0.7	1.8 ± 0.4	>0.99
Cognitive (0–4)	1.6 ± 1.0	2.2 ± 0.7	0.246
Urinary (0–4)	1.5 ± 0.7	1.6 ± 1.0	0.832
TUG (sec)	17.6 ± 4.6	37.2 ± 39.0	0.316
MMSE (0–30)	25.2 ± 4.7	20.8 ± 3.9	0.043
FAB (0–18)	12.7 ± 2.6	10.4 ± 2.9	0.127
TMT-A (sec)	144 ± 107	128 ± 57	0.868
CSF			
Pressure (cm H ₂ O)	16.0 ± 3.3	14.4 ± 3.9	0.632
Protein (mg/dl)	40.8 ± 21.9	46 ± 21.8	0.510
Tap test responders	9 (60)	0 (0)	0.044

Boldface type indicates statistical significance.

* Values expressed as mean ± SD except for responders to the CSF tap test (n, %).

† All p values obtained using the Mann-Whitney U-test except for responders to the CSF tap test (Fisher's exact test).

of iNPH, 5 patients (25%) received shunts and their symptoms improved. All of these patients were included in the CAP group (Supplemental Fig. 2).

Quantification of rCBF in CAP and NCAP

No significant differences between CAP and NCAP were found in the rCBFs of the paracentral lobule (left, $p = 0.60$; right, $p = 0.57$), superior parietal lobule (left, $p = 0.67$; right, $p = 0.55$), or precuneus (left, $p = 0.57$; right, $p = 0.69$; Table 3). The mean rCBFs of these 3 parts of the high-convexity area in CAP patients were in the range of 35.2–43.7 ml/min/100 g. The multicenter validation study of 10 Japanese institutions using the ^{123}I -IMP-ARG method by Iida and colleagues indicated that the mean rCBF

TABLE 3. Summary of rCBF values in study 1

Area*	CAP (n = 15)	NCAP (n = 5)	p Value
Paracentral lobule			
Lt	40.2 ± 7.7	38.7 ± 7.5	0.60
Rt	39.8 ± 7.7	37.2 ± 7.6	0.57
Superior parietal lobule			
Lt	35.2 ± 6.5	36.8 ± 7.0	0.67
Rt	35.9 ± 8.5	37.8 ± 7.6	0.55
Precuneus			
Lt	42.5 ± 8.4	40.5 ± 7.5	0.57
Rt	43.7 ± 9.9	41.8 ± 8.8	0.69

rCBF values given in mg/min/100 g; p values obtained using the Mann-Whitney U-test.

* Areas defined as the high-convexity area in Talairach Daemon Level 3 according to the SEE method.

of the cortical gray matter in 76 healthy subjects was 43.9 ± 3.3 ml/min/100 g.⁶ Moreover, Takaya and colleagues reported that the mean rCBF of the high-convexity area in 7 normal elderly controls (mean age 74.0 ± 4.9 years) was 47.4 ± 10.5 ml/min/100 g using the ^{123}I -IMP-ARG method.²⁶ Therefore, the mean rCBFs of the areas corresponding to the high-convexity area determined in study 1 in the CAP group were within the range of or below the mean rCBF of the cortical gray matter reported by Iida et al. and Takaya et al., demonstrating that there was no real hyperperfusion in the high-convexity area of CAP patients.

Study 2

Patients with iNPH and their clinical features are summarized in Table 4. In CBF SPECT images, the CAPPAAH sign was positive in 24 (80%) of the 30 patients with

TABLE 2. Clinical and laboratory data of the CAP and NCAP groups at 7 days after CSF drainage and clinical changes on the CSF tap test

Variable	CAP (n = 15)	NCAP (n = 5)	p Value
7 days after CSF drainage			
TUG (sec)	16.4 ± 4.6	58.6 ± 58.3	0.014
MMSE (0–30)	25.5 ± 3.8	21.0 ± 3.1	0.050
FAB (0–18)	13.1 ± 2.9	10.8 ± 3.5	0.273
TMT-A (sec)	131 ± 108	131 ± 40	0.536
CSF tap test			
TUG (sec)	−2.9 ± 3.8	8.9 ± 11.4	0.025
MMSE (0–30)	0.3 ± 2.1	0.2 ± 1.2	0.050
FAB (0–18)	0.3 ± 1.4	0.4 ± 1.5	0.893
TMT-A (sec)	−11.7 ± 27.7	−13.7 ± 56.9	0.751

p values obtained using the Mann-Whitney U-test.

TABLE 4. Demographic and clinical characteristics of the participants in study 2

Characteristic	iNPH Patients (n = 30)	Normal Controls (n = 19)	p Value
Mean age ± SD in yrs	75.9 ± 5.9	75.1 ± 7.1	0.47*
Female (%)	12 (40)	10 (53)	0.55†
iNPH diagnosis (%)			
Definite	8 (27)	—	—
Probable	22 (73)	—	—
Symptoms (%)			
Cognitive impairment	23 (77)	—	—
Gait disturbance	29 (97)	—	—
Urinary incontinence	19 (63)	—	—
Imaging findings (%)			
Tight high convexity on MRI	24 (80)	0 (0)	<0.001†

* Mann-Whitney U-test.

† Fisher's exact test

TABLE 5. Summary of CBF SPECT and 3D-SSP images in study 2

Imaging	iNPH Patients (n = 30)	Healthy Controls (n = 19)
CBF SPECT		
CAPPAH sign (+)	24	0
CAPPAH sign (-)	6	19
3D-SSP		
CAPPAH sign (+)	17	0
CAPPAH sign (-)	13	19

iNPH (Table 5), while none of the healthy controls showed the sign. The sensitivity and specificity for the diagnosis of iNPH based on the sign were 80% and 100%, respectively. In 3D-SSP images, the CAPPAH sign was positive in 17 (56.7%) of the 30 patients with iNPH, while none of the healthy controls showed the sign. The sensitivity and specificity for the diagnosis of iNPH by the sign were 56.7% and 100%, respectively. The sensitivity was lower in 3D-SSP than in CBF SPECT images. Moreover, the coincidence rate between tight high convexity on MRI and the CAPPAH sign was very high (Table 6). Nine patients with iNPH received shunts within 3 months after undergoing SPECT (Supplemental Fig. 3). Seven patients showed the CAPPAH sign and a favorable response to shunt surgery. The other 2 patients did not show the CAPPAH sign. One of them showed a poor response to shunt surgery. The sensitivity and specificity for the response to shunt surgery based on the sign were 87.5% and 100%, respectively.

Discussion

Evaluation of Apparent Hyperperfusion by ¹²³I-IMP-ARG Methods

Study 1 demonstrated that the quantitative rCBF was not increased in the high-convexity area of patients with iNPH. There have been some reports on the quantification of rCBF in patients with iNPH using SPECT,^{26,27} but none of the studies focused on the rCBF in the high-convexity area. Takaya and colleagues compared the rCBFs of 35 regions of interest (ROIs) in patients with iNPH, those with preclinical iNPH, and normal controls to determine whether rCBF is associated with the symptoms.²⁶ These authors indicated that the rCBFs of the ROIs corresponding to the high-convexity area were decreased in patients with iNPH. This is consistent with our result that the real rCBF in the high-convexity area was not increased.

There have been various reports on SPECT findings in

iNPH patients without quantification. Some researchers reported frontal-dominant or diffuse CBF reduction in patients with iNPH.^{15,18,24} Others suggested that patients with iNPH showed no specific pattern of SPECT findings.²⁹ In contrast, 2 groups reported that the rCBF of patients with iNPH was relatively increased in the medial frontal, parietal, and occipital lobes, including the high-convexity area.^{9,14} However, neither study analyzed SPECT images using a quantitative method.

Clinical Significance of the CAPPAH Sign

In study 1, the NCAP group, who exhibited DESH findings but did not show a CAPPAH sign, had lower MMSE scores and weaker responses to the CSF tap test. There could be several reasons for these results. First, NCAP might be associated with other diseases. Previous studies investigated the prevalence of an Alzheimer's disease pathology in patients with iNPH.^{2,3} Hamilton and colleagues reported that cortical tau and amyloid β accumulations were associated with poorer outcomes following shunt surgery.³ In CBF SPECT images, hypoperfusion of the parietal lobes, which is common in patients with Alzheimer's disease,¹⁹ might make the CAPPAH sign indistinct in patients with iNPH if they have the Alzheimer's disease pathology. Secondly, DESH findings of the participants could not be precisely determined in some cases. In such cases, the CAPPAH sign could be useful as a supportive diagnostic method for high-convexity tightness.

No consensus has been reached regarding whether SPECT images could be used to predict the resolution of symptoms after shunt surgery.⁹ No previous reports evaluated whether apparent hyperperfusion of the high-convexity area was associated with the response to shunt surgery. Our results suggest that a negative CAPPAH sign in iNPH patients with DESH could be a predictor of a poor response to the CSF tap test and probably to shunt surgery.

Assessment of the CAPPAH Sign by SPECT Images

In study 2, the CAPPAH sign was positive only in patients with iNPH (24/30) and not in controls. The CAPPAH sign was less sensitively detected in 3D-SSP compared with CBF SPECT images. The rCBF of the cortical gray matter is approximately 2.5 to 4 times higher than that of the white matter, and the CSF space has no blood flow.⁸ In CBF SPECT images, which show average counts for each pixel, the tight high-convexity area of patients with iNPH is believed to show apparent hyperperfusion because the pixels of compressed areas include a large amount of gray matter and small CSF space. In contrast, in 3D-SSP images, the peak activity of the 6 pixels (13.5 mm) perpendicular to the cortical surface is projected onto the predefined surface pixel and defined as the count of each surface pixel. Thus, 3D-SSP images may be less affected by the decrease in the CSF space in some pixels of all the analyzed areas and would accordingly show similar images to the real CBF maps. As a result, we consider that CBF SPECT images are more sensitive than 3D-SSP images for the detection of the CAPPAH sign because it is a sign of apparent and not real hyperperfusion.

TABLE 6. Contingency table showing the presence of tight high convexity and CAPPAH sign

CAPPAH Sign	Tight High Convexity	
	(+)	(-)
(+)	23	1
(-)	1	5

Limitations of the Study

The small sample size of patients with iNPH, especially NCAP, may limit the generalizability of the findings. Another limitation is that not all of the patients with iNPH had shunts placed (5 of 20 in study 1, 9 of 30 in study 2). However, we conducted the CSF tap test, which shows very high-level specificity for predicting the effect of shunt surgery.¹⁷ Further studies with a greater number of SPECT images of patients with iNPH who have shunts placed may strengthen our findings.

Conclusions

The quantitative study using the ¹²³I-IMP-ARG method suggested that the CAPPAAH sign did not show real hyperperfusion of the high-convexity area. Nevertheless, patients with iNPH exhibited apparent hyperperfusion of the high-convexity area in CBF SPECT images. We considered the CAPPAAH sign to be useful in the diagnosis of iNPH, and a negative CAPPAAH sign in patients with DESH findings might indicate comorbidities that influence the rCBF in the parietal cortices, such as Alzheimer's disease.

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Disclosures

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Author Contributions

Conception and design: Kondo, Tokuda. Acquisition of data: Ohmichi, Itsukage, Koizumi. Analysis and interpretation of data: Kondo, Ohmichi, Matsushima, Tokuda. Drafting the article: Kondo, Ohmichi, Tokuda. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kondo. Statistical analysis: Ohmichi, Kuriyama. Study supervision: Ishii, Mori, Yamada, Mizuno, Tokuda.

Supplemental Information

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