Grooved pegboard test performance before and after cerebral-spinal fluid tap test in patients with normal pressure hydrocephalus

Caiyan Liu
Peking Union Medical College Hospital https://orcid.org/0000-0001-6035-7456
Liling Dong
Peking Union Medical College Hospital
Chenhui Mao
Peking Union Medical College Hospital
Jie Li
Peking Union Medical College Hospital
Xinying Huang
Peking Union Medical College Hospital
Junji Wei
Peking Union Medical College Hospital
Bo Hou
Peking Union Medical College Hospital
Feng Feng
Peking Union Medical College Hospital
Liying Cui
Peking Union Medical College Hospital
Jing Gao (gj107@163.com)
Department of Neurology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences

Research

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Abstract

Background Motor impairment in patients with normal pressure hydrocephalus (NPH) can extend beyond gait and include deficits in upper extremity functions and psychomotor speed. Evaluation of upper extremity function will be helpful for NPH patients who are unable to ambulate (e.g., wheelchair-bound patients) and may not be able to comply with the gait evaluation. Our study aimed to explore the use of the grooved pegboard test to assess responsiveness to the cerebrospinal fluid (CSF) tap test in patients with NPH.

Methods Seventy-five possible NPH patients were enrolled from 2012 to 2018. All patients underwent detailed neuropsychological and walking assessments, CSF tap tests, and brain magnetic resonance imaging. The grooved pegboard test results before and after the CSF tap test were compared and correlated with the other clinical assessments. In diffusion tensor imaging analysis, the fractional anisotropy (FA) and mean diffusivity (MD) values of periventricular white matter were measured by the region of interest method and were correlated with pegboard test performance.

Results The grooved pegboard test scores significantly improved after the CSF tap test and correlated with patient walking ability, cognitive function, and functional scores ($P < 0.01$). The improvement ratios in the complex visual motor speed index (i.e., the grooved pegboard test performance combined with the Symbol-Digit Modalities Test performance) were significantly different between the CSF tap test responder and nonresponder groups. The grooved pegboard test times were significantly correlated with the FA values in right periventricular lesions ($P=0.017$).

Conclusions The performance on the grooved pegboard test was related to lower extremity motor ability and cognitive function. It can be used as an alternative evaluation tool for patients who are unable to ambulate and may not be able to comply with the gait evaluation.

Background

Normal pressure hydrocephalus (NPH) patients present disturbances in gait and balance, cognition and/or control of urination with neuroimaging characterized by enlargement of the cerebral ventricles [1–3]. Typically, gait disturbance in NPH patients is the initial and most prominent symptom [4, 5], but motor impairments can also extend to include upper extremity dysfunction [6–9]. Cognitive impairment in NPH patients is generally characterized by frontal system deficits that may include slowing of information processing, task shifting, reduced learning and executive abilities [10-12]. Bladder control dysfunction can range from increased urinary urgency and frequency to frank incontinence [13].

A commonly used auxiliary test for predicting shunt responsiveness is the cerebrospinal fluid (CSF) tap test (TT), a procedure in which NPH symptoms are assessed before and after drainage of 30～50 cm3 of CSF by lumbar puncture. Clinical improvement following lumbar puncture indicates an increased likelihood of improvement after shunt placement [14-16]; however, a negative CSF TT does not rule out shunt responsiveness [17]. Standard methods for determining the CSF TT response are based on the

clinical impression of changes in gait and cognition after lumber puncture. Instruments to evaluate gait [18, 19] can be useful in this assessment but are not always sensitive to subtle changes. NPH patients who are unable to ambulate (e.g., the patient is wheelchair bound) may not be able to comply with the gait evaluation but still benefit from shunt placement. In mildly affected patients, testing may not reveal sufficiently profound impairments to permit assessment of change after a lumber puncture. Therefore, we sought to identify additional measures that can be used to objectively assess responsiveness to the CSF TT.

The grooved pegboard test assesses eye-hand coordination and motor speed and thus requires sensory-motor integration and a high level of motor processing [20]. It is considered a more complex motor task than others, such as grip strength or finger tapping. As such, it requires more effort and is more sensitive to psychomotor speed [21]. The test has been used extensively for identifying lateralized impairments such as those in Parkinson's disease. In NPH patients, some researchers have used grooved pegboard performance as a psychometric measure for upper extremity motor and psychomotor speed [22]. Upper extremity motor tests may be particularly advantageous in situations where the severity of impairment precludes accurate and reliable assessments of changes in gait.

Herein, we performed a pilot study to investigate changes in grooved pegboard performance before and after CSF TT and its correlation with clinical parameters and white matter lesions and to explore the possibility of its application in combination with the CSF TT.

Methods

Patients, history taking and clinical assessment

We retrospectively reviewed the patients (n = 137) with possible NPH who were admitted in neurological or neurosurgery department ward of Peking Union Medical College Hospital for the CSF tap test. All the patients were diagnosed as possible NPH according to the guidelines for the clinical diagnosis of idiopathic NPH (INPH) published in 2005 [23] and Chinese consensus for iNPH [24].

In the CSF tap test and NPH registry protocol, age, gender, past histories, personal histories, and initial and full-blown symptoms for all patients were recorded. Patients also completed the Mini-Mental State Examination (MMSE) [25], Montreal Cognitive Assessment (MOCA) [26], and activities of daily living (ADL) questionnaire [27]. And they also underwent the brief executive function battery assessment including the Symbol-Digit Modalities Test [28], Trail Making Test A [29] and the Stroop Color Word Task-C(SCWT) [30] . The iNPH Grading Scale (iNPHGS) [31] was used to rate the severity of each fundamental symptom of iNPH (gait disturbance, cognitive impairment, and urinary incontinence) on a four-point scale after a detailed interview with the patients and caregivers. All subjects underwent a CSF TT and brain MRI. The NPH diagnosis and treatment paradigm in Peking Union Medical College Hospital was detailed in Figure 1a.

The CSF TT was performed by lumbar puncture followed by the measurement of CSF opening pressure and drainage 30 ml CSF. Before and after the procedure, cognitive function and walking ability were evaluated by the means of 5-meter up and go test (TUG), the 10-meter walking test, the grooved pegboard test and a brief executive function battery, which was previously described [32]. The time of TUG and the time and steps that the patient took to complete the 10-meter walking test and a video of the walking tests were recorded. Additional evaluations were conducted at 8 hours, 24 hours and 72 hours after CSF TT. In addition to the walking and cognitive function evaluation, the urinary and fecal function questionnaire was completed by the caregiver and patients. The total symptom improvement questionnaire was evaluated by the caregiver and patients at the same time. The following criteria were used to identify responders: 1. CSF TT responders were defined as patients with reductions in their time and number of steps in the walking test at least once after the CSF TT, with decreases of 10% for both parameters or a decrease of 20% on at least one of these parameters [33]. 2. Gait was improved based on videos that were evaluated by two neurologists who were blinded to the patient's clinical and neuroimaging characteristics. 3. The total symptom improvement questionnaire scores were partly or obviously improved. The patients who met 2 of 3 criteria were identified as CSF TT responders.

The inclusion and exclusion criteria

The patients were recruited in the study according to the following criteria: 1. the patients had to be older than 40 years of age; 2. the patients completed the multi-time point assessment of walking and neuropsychological tests; 3. The patients had underwent at least 3 times testing of the grooved pegboard test including baseline. The exclusion criteria as follows: 1. non-communicating hydrocephalus; 2. Patients weren't able to finish the grooved pegboard test for any reason. 3. The patients could not tolerate 30 ml CSF drainage during CSF TT.

Brain MRI

Axial and sagittal spin-echo T1-weighted images, axial fast spin-echo T2-weighted, fluid-attenuated inversion recovery images were obtained by using a 1.5-T MRI unit (Signa Excite, General Electric, Milwaukee, WI, USA). Diffusion tensor imaging (DTI) is one selected test for patients. We obtained and analyzed 22 patients' DTI data at last. The ROIs were the bilateral anterior and posterior periventricular white matter that were set as circular areas with a diameter of 2 mm perpendicular to the longitudinal axis of the ipsilateral ventricle on the brain imaging slice with the lateral ventricle (detailed in Figure 2). The fractional anisotropy (FA) and mean diffusivity (MD) values were measured across regions of interest (ROIs) on DTI images. The ROIs were chosen according to our pilot study data [34], which indicated that the FA and MD values in the bilateral anterior and posterior periventricular white matter were correlated with walking ability and cognition in possible NPH patients. A consistency test was performed (Cronbach's a coefficient > 0.6).

Statistical methods

If the data conformed to a normal distribution, the data are presented as the mean ± standard deviation; if the measurement data conformed to a skewed distribution, the data are presented as the median (interquartile range). The scores for various evaluation indexes before and 8 hours, 24 hours and 72 hours after CSF TT conformed to skewed distributions. The differences in the grooved pegboard test results before and after the CSF TT were analyzed using a nonparametric paired sign rank-sum test. The grooved pegboard test results at the three different time points after the CSF TT (i.e., 8 hours, 24 hours and 72 hours) were also compared by means of a nonparametric paired sign rank-sum test. There were four time assessments related to the CSF TT, and the Bonferroni correction was applied for the repeated measurements. The statistical significance level was set at $p<0.05/4=0.01$.

We compared the maximum improvement ratios for the grooved pegboard test and Symbol-Digit Modalities Test performance, between the CSF TT responder and non-responder groups by means of the Mann-Whitney U test. The improvement ratio was calculated as follows: (baseline performance on the grooved pegboard test - performance after CSF TT) / the baseline performance. The maximum improvement ratio for the grooved pegboard test was calculated for the different times (i.e., 8 hours, 24 hours, and 72 hours) after CSF TT. The improvement ratio of the grooved pegboard test and Symbol-Digit Modalities Test performance were combined into the improvement ratio of the complex visual motor speed index [22]. The formula was: the improvement ratio of the complex visual motor speed index = (the improvement ratio of Symbol-Digit Modalities Test raw score + the improvement ratio of mean performance of bilateral grooved pegboard test)/2. The improvement ratio for the complex visual motor speed index after CSF TT was also compared between the responder and nonresponder groups using the Mann-Whitney U test. The statistical significance level was set at $p<0.05$.

The correlations between the grooved pegboard test results and the iNPHGS scores, walking test results, and neuropsychological performance were tested by means of Spearman correlations. The correlations between the improvement ratio of the grooved pegboard test and that of the walking test, between improvement ratio of the complex visual motor speed index and that of the walking test post CSF TT were also tested by means of Spearman correlations. And the correlations between the grooved pegboard test results and the DTI parameters from the periventricular white matter lesions were also analyzed using the Spearman correlation method. The statistical significance level was set at $p<0.05$.

All statistical analyses were performed with the statistical software package SPSS for Windows (version 13.0.; SPSS Inc., Chicago, IL, USA).

Results

Demographic characteristics of CSF TT responders and nonresponders

Seventy-five NPH patients were recruited for this study. Among them, there were 67 patients diagnosed as idiopathic NPH and 8 patients diagnosed as secondary NPH patients. And there were 3 patients secondary to trauma, 2 patients secondary to infection, 1 patient secondary to autoimmune disease, 1 patients secondary to subarachnoid hemorrhage and 1 patient secondary to neoplasm. There were no

significant differences in age, gender, disease duration, iNPHGS, MMSE, MOCA scores and 10 meter walking time, but there was a difference with the ADL scores (Table 1) between the CSF TT responders and non-responders group.

Among the 75 possible NPH patients, 23 patients had shunting surgery. 19/23 patients were followed up until May, 2019. The follow-up time was (2.8±1.8) year. 68% (13/19) patients showed improvement of clinical symptoms after shunting surgery, while 32% (6/19) patients had no improvement or experienced clinical deterioration. And 12/19 patients were tap test responder according to our criteria. The predictive effect of grooved pegboard test on the shunting response hadn't been analyzed for the limited sample.

The grooved pegboard test performance changes from before to after the CSF TT

The bilateral grooved pegboard test results at 24 hours and 72 hours after the CSF TT were significantly improved compared with those before the CSF TT (P<0.01) (Table 2). We also tested the grooved pegboard test result differences at 8 hours, 24 hours and 72 hours after the CSF TT. There were significant differences among the three time points with the nondominant hand. With the dominant hand, there were significant differences at 8 hours vs. 72 hours and at 24 hours vs. 72 hours after CSF TT. (Table 2)

Two iNPH patients who didn't undergo the CSF tap test were tested using the same protocol and the cognitive tests results didn't show learning effect what was concerned about. (Supplementary material 1)

Comparison of the changes in grooved pegboard test results between the CSF TT responders and nonresponders

We compared the maximum improvement ratios for the grooved pegboard test, the Symbol-Digit Modalities Test and the complex visual motor speed index between the CSF TT responder and nonresponder groups after the CSF TT. The maximum improvement ratio of the index for the CSF TT responders and nonresponders was also compared after the CSF TT. There was a significant difference on the maximum improvement ratio of the complex visual motor speed index between the two groups (U=327, P=0.02) (Figure 3). The maximum improvement ratios for the grooved pegboard test, the Symbol-Digit Modalities Test tended to be different between the two groups(U=516, 367,respectively; P=0.06, 0.06, respectively)

Correlations between baseline grooved pegboard test performance and clinical parameters, between the improvement ratio of the grooved pegboard test, the complex visual motor speed index post CSF TT and the improvement ratio of the walking test

The baseline mean bilateral grooved pegboard test results correlated significantly with the baseline INPHGS total, INPHGS walking, INPHGS cognition, MMSE, MOCA and ADL scores and 10-meter walking test times (Rho=0.41, 0.48, 0.30, -0.48, -0.54,0.61, respectively, P<0.01) and did not correlate with the INPHGS urinary score (Rho=0.17, P=0.13)

We also correlated the improvement ratio of the grooved pegboard test, the complex visual motor speed index post CSF TT with the improvement ratio of the TUG, 10 meter walking time and steps. The results showed the improvement ratio of the grooved pegboard test and the complex visual motor speed index on 72hr post CSF TT was significantly correlated with TUG time improvement ratio at the same time point. Detailed in Table 3

Correlations between grooved pegboard test performance and the periventricular white matter lesion DTI parameters in possible NPH patients

Twenty-two patients underwent DTI evaluation. The bilateral grooved pegboard test performance correlated with the right periventricular anterior horn FA values (right: rho=0.48, P=0.04, left: rho=-0.55, P=0.02). The right grooved pegboard test results correlated with the left periventricular anterior horn MD values. There were no significant correlations between the grooved pegboard test results and periventricular posterior horn FA and MD values.

Discussion

The present findings demonstrate that upper extremity motor functions can improve following TT, providing an additional measure of a clinical response. The pegboard test results correlated with cognition and lower extremity motor function. The improvement ratios for the complex visual motor speed index (the grooved pegboard test performance combined with the Symbol-Digit Modalities Test performance) were significantly different between the CSF TT responder and nonresponder groups. Additionally, the results from the pegboard test were correlated with periventricular white matter lesion DTI parameters.

Upper extremity function is impacted in NPH patients, although lower extremity motor function is the primary concern in NPH patients. There have been several studies on upper extremity motor function after CSF drainage tests and shunting operations in iNPH patients. Tsakanikas D et al reported that these upper extremity motor tests may be useful as sensitive markers of change after shunt placement in iNPH patients (e.g., line tracing tasks) [22]. Kang et al reported the upper limb motor function was improved after CSF TT and shunting and correlated with the gait parameters [7]. Liouta E et al also found that finger tapping improvements after CSF TT were useful for the differential diagnosis and prediction of shunt treatment outcomes [35]. The strength of our study was the multiple time point assessments of the upper extremity motor function. And we found that the complex visual motor speed index (a combined measure of grooved pegboard test and Symbol-Digit Modalities Test performance) was more useful in demonstrating significant differences between the CSF TT responder and nonresponder groups. The complex visual motor speed index might be a promising candidate measure to recognize CSF TT responders. Tsakanikas D mentioned that there was no significant decrease in the complex visual motor speed index after CSF TT [22]. However, they performed the evaluation just once, at 2-4 hours after CSF TT, which might have missed the time point showing the best improvement.

Our study also provided evidence on correlations between the grooved pegboard test performance and cognition and walking ability in patients with NPH. And the improvement ratio of the grooved pegboard test on 72hr after CSF TT was significantly correlated with TUG improvement ratio on 72hr after CSF TT. The correlation of walking and executive neurocognitive deficits has been reported in NPH patients and supports the notion that gait deficits are due to executive motor planning dysfunction [36]. Upper extremity motor function seems to be consistent with changes in walking ability and cognition, which indicates common mechanisms of motor disturbance and cognitive impairment in NPH patients. This relationship also supported the notion that the grooved pegboard test can be a reliable and useful assessment tool for NPH patients.

The correlation of grooved pegboard test results with the DTI parameters of the periventricular white matter lesions provided mechanistic evidence of upper limb motor dysfunction in NPH patients. White matter lesions are very common in NPH patients. The reduction in the irregular type of periventricular hyperintensity located around the frontal horns after surgery has been reported to be associated with clinical improvements in patients with iNPH [37]. The DTI technique can provide good markers of white matter pathology. Some researchers have reported that brain white matter regions in which FA was decreased after shunt placement were in the corona radiata between the lateral ventricles and the Sylvian fissures in NPH patients [38]. Our study results demonstrated that the grooved pegboard test results for both hands correlated to the right side FA values in white matter lesions on the anterior periventricular horn. This is consistent with the previous literature and provides more data on the mechanism of motor dysfunction in patients with NPH.

Conclusions

Our study reported that the performance on the grooved pegboard test was related to lower extremity motor ability and cognitive function. The improvement ratios for the complex visual motor speed index (the grooved pegboard test performance combined with the Symbol-Digit Modalities Test performance) were significantly different between the CSF TT responder and non-responder groups. It might be used as an alternative evaluation tool for patients who are unable to ambulate and may not be able to comply with the gait evaluation.

Limitations

Our study has several limitations. First, the sample size of patients undergoing surgery was small, and the prediction of the grooved pegboard test was not investigated. Second, this is a pilot study, and the grooved pegboard test results were analyzed among the patients with NPH who completed the multiple time point evaluation after CSF TT. The application of the grooved pegboard test in patients who are unable to ambulate needs to be explored in the future.

Abbreviations

iNPH: idiopathic normal pressure hydrocephalus; CSF: cerebrospinal fluid; NPH: normal pressure hydrocephalus; MRI: magnetic resonance imaging; CSF TT: cerebrospinal fluid tap test; MMSE: Mini-Mental State Examination; MOCA: Montreal Cognitive Assessment; ADL: activities of daily living questionnaire; iNPHGS: iNPH Grading Scale; DTI: diffusion tensor imaging; FA: The fractional anisotropy; MD: mean diffusivity; ROIs: regions of interest; ml: milliliter.

Declarations

Authors' contributions

Caiyan Liu and Jing Gao drafted and revised the manuscript, contributed to the data analysis and interpreted results. Study was designed by Caiyan Liu and Jing Gao. Study supervision and obtaining study funding by Jing Gao and Liying Cui. Caiyan Liu, Liling Dong, Chenhui Mao, Jie Li, Xinying Huang contributed to the clinical assessment and data acquisition. Bo Hou, Feng Feng were responsible to the neuroimaging data collection and analysis. Junji Wei contributed to the neurosurgery treatment for patients. Caiyan Liu performed the statistical analysis. All authors read and approved the final manuscript.

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Availability of data and materials

The anonymized datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The permission for the research was received from the Research Ethics Board of the Peking Union Medical College Hospital (PUMCH). Informed consent was obtained from every patient or a legally authorized representative before undergoing evaluations.

Consent for publication

Personal information is de-identified in this manuscript.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Neurology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, No.1 Shuaifuyuan, Wangfujing St., Beijing, China, 100730. [2]Department of Neurosurgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China
[3]Department of Neurosurgery and Radiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China

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Tables

Table 1

Demographic characteristics of the CSF TT responder and nonresponder groups

	Responders (n = 42)	Nonresponders (n = 33)	P value
Age (years old)	68 ± 12	68 ± 11	0.82
Gender (male:female)	34:8	26:7	0.94
Duration (years)	3.8 ± 3.3	3.6 ± 2.8	0.76
iNPHGS total	5.8 ± 1.6	5.2 ± 2.2	0.21
MMSE	20.5 ± 7.3	22.9 ± 6.0	0.23
MOCA	17.3 ± 7.1	18.1 ± 6.6	0.71
ADL	41.2 ± 14.5	30.0 ± 9.5	0.01*
10-meter walking time (seconds)	23.4 ± 28.6	39.2 ± 130.0	0.45

*P < 0.05

Table 2 Comparison of the grooved pegboard test (GPT) results before and after the CSF TT

	GPT–nondominant hand（Median （Inter Quartile Range））	Z	P	GPT–dominant hand（Median （Inter Quartile Range））	Z	P
Baseline	141.0 (143)			130.2 (113.5)		
8 hr after CSF TT	134.5 (136.5)	-1.63[1]	0.10[1]	123.0 (90.0)	-2.41[4]	0.02[4]
24 hr after CSF TT	131.8 (133.4)	-4.21[1]	0.00[1]*	121.4 (101)	-3.04[4]	0.00[4]*
		-2.46[2]	0.01[2]*		-1.97[5]	0.05[5]
72 hr after CSF TT	120.3 (93.2)	-5.38[1]	0.00[1]*	118.0 (92.7)	-3.80[4]	0.00[4]*
		-4.84[2]	0.00[2]*		-3.07[5]	0.00[5]*
		-4.40[3]	0.00[3]*		-2.59[6]	0.01[6]*

Note: *P<0.01

[1] compared to the baseline GPT result with the nondominant hand

[2] compared to the GPT result with the nondominant hand at 8 hr after the CSF TT

[3] compared to the GPT result 24 hr after the CSF TT

[4] compared to the baseline GPT result with the dominant hand

[5] compared to the GPT result with the dominant hand 8 hr after the CSF TT

[6] compared to the GPT result with the dominant hand 24 hr after the CSF TT

Table 3 The correlation of improvement ratio of the grooved pegboard test and complex visual motor speed index with the walking test result.

	Spearman Rho	P value
Correlation of 8hr improvement ratio of grooved pegboard test with		
8hr improvement ratio of TUG time	0.101	0.402
8hr improvement ratio of 10Ti	-0.07	0.95
8hr improvement ratio of 10St	0.055	0.648
Correlation of 24hr improvement ratio of grooved pegboard test with		
24hr improvement ratio of TUG time	0.067	0.57
24hr improvement ratio of 10Ti	0.186	0.113
24hr improvement ratio of 10St	0.222	0.057
Correlation of 72hr improvement ratio of grooved pegboard test with		
72hr improvement ratio of TUG time	0.310	**0.01***
72hr improvement ratio of 10Ti	0.135	0.271
72hr improvement ratio of 10St	0.217	0.075
Correlation of 8hr improvement ratio of complex visual motor speed index with		
8hr improvement ratio of TUG time	0.07	0.617
8hr improvement ratio of 10Ti	0.01	0.96
8hr improvement ratio of 10St	0.197	0.131
Correlation of 24hr improvement ratio of complex visual motor speed index with		
24hr improvement ratio of TUG time	0.161	0.207
24hr improvement ratio of 10Ti	0.188	0.140
24hr improvement ratio of 10St	0.173	0.175
Correlation of 72hr improvement ratio of complex visual motor speed index with		
72hr improvement ratio of TUG time	0.272	**0.035***
72hr improvement ratio of 10Ti	0.139	0.290
72hr improvement ratio of 10St	0.249	0.056

Note: TUG: The timed Up and Go test, 10Ti: 10 meter walking time, 10St: 10 meter walking steps.

*P<0.05

Figures

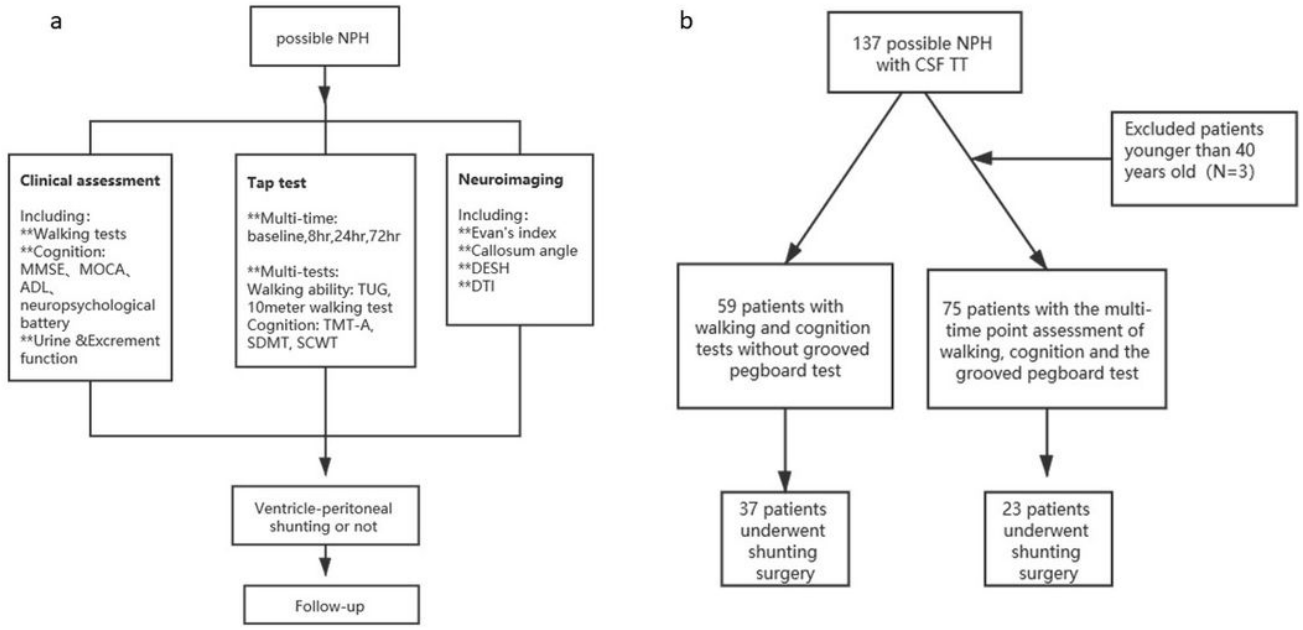

Figure 1

The flow-chart describing the NPH diagnosis and treatment paradigm and the patients recruitment. a:The NPH diagnosis and treatment paradigm in Peking Union Medical College Hospital was showed. b: The flow-chart described the recruitment of NPH patients. Abbreviation: MMSE: Mini-Mental State Examination; MOCA: Montreal Cognitive Assessment; ADL: Activities of daily living; TUG: Up and GO test; TMT-A: Trail-making test-A; SDMT: Symbol-Digit Modalities Test; SCWT: the Stroop Color Word Task; DESH: Disproporation enlarged subarachnoid hydrocephalus; DTI: Diffusion tensor imaging.

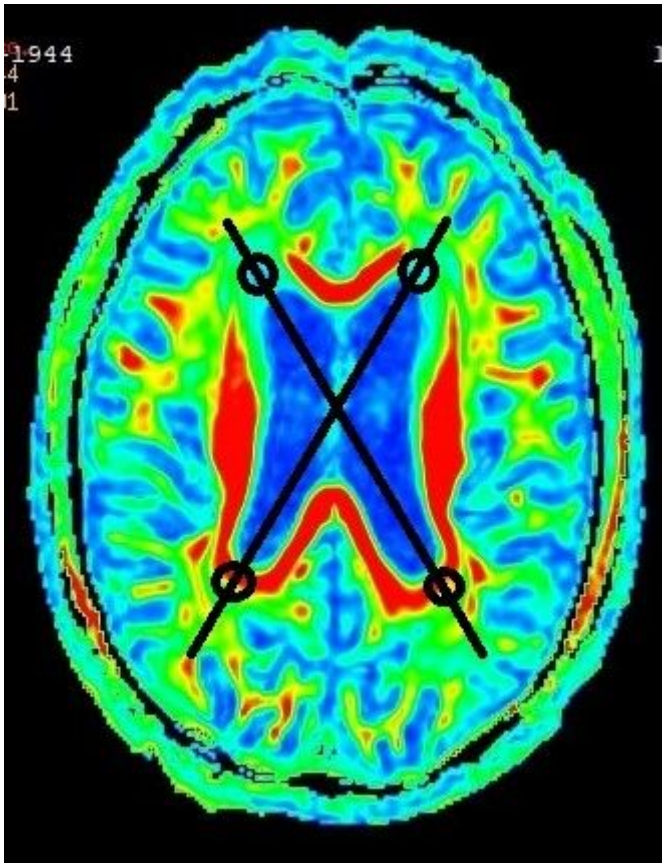

Figure 2

The diffusion tensor imaging illustrates the location of the region of interest(ROI)s. ROIs were the bilateral anterior and posterior periventricular white matter that were set as circular areas with a diameter of 2 mm perpendicular to the longitudinal axis of the ipsilateral ventricle on the brain imaging slice with the lateral ventricle.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarymaterial1.docx