



Clinical short communication

## Can the radiological scale “iNPH Radscale” predict tap test response in idiopathic normal pressure hydrocephalus?

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## ABSTRACT

**Background:** Idiopathic normal pressure hydrocephalus (iNPH) presents typical radiological signs that have been summarised in a semi-quantitative scale named the iNPH Radscale. However, the iNPH Radscale's predictive value for response to cerebrospinal fluid (CSF) tap test has never been studied. This study aims to investigate if the iNPH Radscale can predict locomotion improvement after CSF tap test.

**Methods:** A total of 100 patients with iNPH (age:  $76.3 \pm 7.9$ , gender: 36% female) were included in this retrospective study. Two raters, blinded to the response of the CSF tap test, evaluated the iNPH Radscale and its seven subitems (Evan's index, callosal angle, size of temporal horns, narrow high-convexity sulci, dilated Sylvian fissures, focally dilated sulci, and periventricular hypodensities). Locomotion improvement was assessed by the Timed Up and Go (TUG) performed before, and 24 h after, the CSF tap test.

**Results:** The iNPH Radscale (total score) was similar between the CSF tap test responders and non-responders (responders:  $8.31 \pm 1.96$ , non-responders:  $9.18 \pm 2.51$ ,  $p = 0.128$ ). However, the temporal horns score was smaller in the responders group ( $1.66 \pm 0.57$  versus  $1.94 \pm 0.24$ ,  $p = 0.045$ ), even after adjusting for age, gender, education level, white matter changes, and global cognition ( $\beta$ :  $-0.250$ , C.I. 95%:  $[-3.185; -0.161]$ ,  $p = 0.031$ ).

**Conclusion:** The iNPH Radscale (total score) does not predict locomotion improvement after CSF tap test, while a smaller temporal horns score at baseline is associated with a positive tap test responder status.

### 1. Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is characterised by locomotion disturbance, cognitive impairment, and urinary incontinence, with enlarged ventricles at brain imaging [1,2]. Its treatment relies on an invasive neurosurgical shunt procedure [3]. iNPH is often associated with comorbid neurological conditions, such as Alzheimer's disease or other neurodegenerative conditions, which interfere with the reversibility of symptoms [4]. Various neuroimaging biomarkers, such as the hippocampal volume or microstructural changes in specific white matter tracts [5,6], have been studied to identify iNPH patients with

good prognosis after shunt surgery. However, these neuroimaging features rely on complex image processing approaches, which are difficult to apply in clinical practice. Furthermore, these neuroimaging biomarkers mainly apply to MRI and not to CT-Scans that are largely performed in iNPH patients.

Recently, the iNPH Radscale – a semi-quantitative radiological scale that includes seven radiological parameters (Evan's index, narrow sulci, Sylvian fissures, focally enlarged sulci, temporal horns, callosal angle, and periventricular hypodensities) – has been validated to identify patients with iNPH [7]. The severity of the iNPH Radscale correlates with the severity of clinical symptoms in iNPH patients [7], and demonstrates

**Abbreviations:** ARWMC, Age-Related White Matter Changes; CSF, Cerebrospinal Fluid; GHS, Global Health Status; HAD, Hospital Anxiety and Depression; ICC, Intraclass Correlation Coefficients; iNPH, idiopathic Normal Pressure Hydrocephalus; MMSE, Mini-Mental State Examination; SD, Standard Deviation; TUG, Times Up and Go.

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high specificity and sensitivity for distinguishing iNPH patients from asymptomatic individuals in the general population [8]. Furthermore, the iNPH Radscale demonstrates a similar validity when assessing brain imaging with CT or MRI [9]. However, the iNPH Radscale and its sub-items have never been studied for their ability to identify iNPH responders from non-responders.

This study aims to investigate if the iNPH Radscale and its subitems can predict if iNPH patients improve their locomotion after cerebrospinal fluid (CSF) tap test (i.e. responders), by using the Timed Up and Go (TUG) – a largely used clinical test that has been also validated in iNPH [10,11]. Establishing this would contribute to the identification of appropriate iNPH candidates for shunt surgery.

## 2. Materials and methods

### 2.1. Sample

A total of 179 consecutive patients enrolled in the Geneva Protocol [12] from September 2009 to February 2019 were selected for this study. The study procedures were previously described [12]. Briefly, inclusion criteria for this analysis were: patients with (i) a diagnosis of possible or probable iNPH that fulfilled the iNPH consensus guidelines criteria [13], (ii) a brain MRI or CT, and (iii) a Timed Up and Go (TUG) test performed before and 24 h after CSF tap testing. Seventy patients were excluded because they were diagnosed with iNPH mimics, and nine due to missing pre or post CSF tap test locomotion assessment. The final sample consisted of 100 patients with a possible or probable iNPH diagnosis. A total of 41 of the 100 patients performed a shunt surgery; 37 of which (90.2%) improved their gait according to the subjective post-operative evaluation from a neurosurgeon at one-year post-shunting. The study protocol was approved by the ethical committee of Geneva University Hospitals. Patients gave informed consent for their participation.

### 2.2. The iNPH Radscale

The iNPH Radscale is a semi-quantitative imaging scale validated to screen for iNPH [7]. Scores range from 0 to 12, with higher values indicating more severe radiological signs. The iNPH Radscale includes seven subitems: Evan’s index, narrow sulci, Sylvian fissures, focally enlarged sulci, temporal horns, callosal angle, and periventricular hypodensities. Details about the method used to evaluate these subitems can be found in the original iNPH Radscale article [7]. In our cohort, iNPH Radscale scores were evaluated by two independent raters (TL and GA) blinded to the CSF tap test responder status.

### 2.3. Tap test responder status

Tap test responder status was defined with the Timed Up and Go (TUG), as the TUG has been validated for evaluating improvement in locomotion in iNPH patients [11,14]. The TUG was measured before, and 24 h after, the CSF tap test. Participants were asked to perform the TUG at their self-selected, normal speed. We used a very sensitive approach for defining the responder status: TUG improvement was defined by any improvement in TUG time 24 h after the CSF tap test, when compared to the pre-CSF tap test TUG. Furthermore, a sensitivity analysis was carried out at TUG improvement cut-offs between 0% and 10%. The formula used to measure TUG improvement (in %) was:

$$\frac{(\text{post tap TUG}) - (\text{pre tap TUG})}{0.5 * [(\text{post tap TUG}) + (\text{pre tap TUG})]} * 100$$

### 2.4. Covariates

The NPH grading scale [15] was used to quantify the severity of iNPH symptoms. Global cognition was evaluated using the Mini-Mental

State Examination (MMSE). Behavioural symptoms were evaluated using the Starkstein for apathy [16] and the Hospital Anxiety and Depression (HAD) scale for depression and anxiety [17]. The Global Health Status (GHS: range 0–10) was defined based on the presence of diabetes, chronic heart failure, arthritis, hypertension, depression, stroke, Parkinson’s disease, chronic obstructive pulmonary disease, angina, and myocardial infarction [12]. White matter lesions were rated with the age-related white matter changes – a validated semi-quantitative scale [18]. Medial temporal lobe atrophy was evaluated using the Scheltens scale (average score) [19–21].

### 2.5. Statistics

Descriptive statistics were compared between responders and non-responders with a Mann-Whitney U test. Multivariate linear regression adjusted for age, gender, education level, white matter changes, and global cognition was performed to assess the association between responder status (independent variable) and temporal horns (dependent variable). All analyses were conducted using SPSS version 25 (IBM Corp., Armonk, NY., USA).

## 3. Results

Table 1 shows the characteristics of tap test responders versus non-responders: 83% of the patients were classified as responders based on TUG improvement after the CSF tap test. Both groups presented similar clinical characteristics, including age, global cognitive performance, disease duration, as well as the extent of white matter lesions. However, tap test responders performed the TUG slower than non-responders before the CSF tap test ( $p = 0.036$ ). Kappa values and intraclass correlation coefficients (ICC) for iNPH Radscale subitems were similar to those reported by Kockum et al. (kappa range: 0.28–1.00 vs 0.35–0.85

**Table 1**  
Clinical characteristics of tap test responders and non-responders.

Variable	Tap Test Responders (n = 83)		Tap Test Non-Responders (n = 17)		p-value <sup>†</sup>
	Mean	SD	Mean	SD	
<b>Demographics:</b>					
Age (years)	76.2	± 7.9	76.6	± 8.3	0.755
Gender (% female)	39.0	± 49.0	24.0	± 43.7	0.240
Disease Duration (months)	41.6	± 46.0	35.3	± 25.7	0.892
Education (years)	11.7	± 3.9	12.8	± 2.6	0.385
Comorbidities - GHS (0–10)	1.5	± 1.1	1.8	± 1.1	0.191
Number of Medications (n)	4.5	± 2.9	4.6	± 2.4	0.766
<b>NPH grading scale:</b>					
Gait (0–4)	2.0	± 0.4	1.9	± 0.6	0.962
Cognition (0–4)	2.1	± 0.5	2.3	± 0.5	0.202
Urinary (0–4)	1.3	± 1.1	0.9	± 0.8	0.351
<b>Gait:</b>					
<i>Timed Up and Go (TUG):</i>					
Pre tap test TUG (s)	28.8	± 28.5	23.7	± 28.1	0.036*
Post tap test TUG (s)	20.2	± 14.4	33.0	± 44.8	0.271
ΔTUG (%) <sup>‡</sup>	–25.9	± 24.0	19.8	± 26.4	<0.001*
<b>Cognition:</b>					
MMSE (0–30)	23.8	± 4.5	23.7	± 4.4	0.826
<b>Behaviour:</b>					
Anxiety (0–21)	7.3	± 3.9	6.4	± 2.3	0.461
Depression (0–21)	7.0	± 3.8	5.8	± 3.0	0.449
Apathy (0–42)	17.1	± 6.0	13.5	± 5.5	0.068
<b>White matter lesions:</b>					
Total ARWMC (0–30)	6.7	± 4.4	8.0	± 5.8	0.438

Abbreviations: ARWMC: Age-Related White Matter Changes; GHS: Global Health Scale; MMSE: Mini-Mental State Examination; SD: standard deviation.

<sup>†</sup> Statistically significant p-values are indicated with a \*.

<sup>‡</sup> ΔTUG is calculated using the formula:  $\frac{(\text{post tap TUG}) - (\text{pre tap TUG})}{0.5 * [(\text{post tap TUG}) + (\text{pre tap TUG})]} * 100$

for Kockum et al.; ICC range: 0.57–1.00 vs 0.74–0.97 for Kockum et al.) [7].

Both groups presented a similar total composite iNPH Radscale score ( $p = 0.128$ ) (Table 2). However, for individual subitems of the iNPH Radscale (Table 2), the tap test responders exhibited a smaller temporal horns score compared to the non-responders ( $p = 0.045$ ). This difference in temporal horns scores (using the semi-quantitative iNPH Radscale), was confirmed by the quantitative measurement of temporal horns width (Fig. 1):  $7.71 \pm 2.47$  mm for the tap test responders, versus  $9.12 \pm 2.29$  mm for the non-responders ( $p = 0.031$ ). This association between smaller temporal horns width and positive tap test responder status remained significant even after adjusting for age, gender, education level, white matter changes, and global cognition ( $\beta$ :  $-0.250$ , C.I. 95%:  $[-3.185; -0.161]$ ,  $p = 0.031$ ). Scheltens' scale for medial temporal lobe atrophy yielded a score of  $1.63 \pm 0.86$  for tap test responders vs  $2.27 \pm 0.99$  for non-responders ( $p = 0.010$ ), and  $1.74 \pm 0.91$  for the entire sample of iNPH patients.

The sensitivity analysis using cut-offs of TUG improvement between 0% and 10% yielded similar results to Table 2. The association between smaller temporal scores and positive tap test responder status was not significant anymore at a cut-off of TUG improvement  $\geq 6\%$ . However, when using a TUG improvement cut-off  $\geq 10\%$  for responders and  $< 0\%$  for non-responders, the results closely resemble those shown in Table 2, including for the temporal horns observation (temporal horns scores  $1.64 \pm 0.61$   $n = 61$  vs  $1.94 \pm 0.24$   $n = 17$ , respectively,  $p = 0.044$ ). Furthermore, all of our findings were similar when defining TUG improvement in % as  $\frac{(\text{post tap TUG}) - (\text{pre tap TUG})}{(\text{pre tap TUG})} * 100$ .

#### 4. Discussion

##### 4.1. Main findings

While the iNPH Radscale (total score) does not predict locomotion improvement after CSF tap test, a smaller temporal horns score – a subitem of the iNPH Radscale – is associated with improvement in locomotion.

##### 4.2. Temporal horns

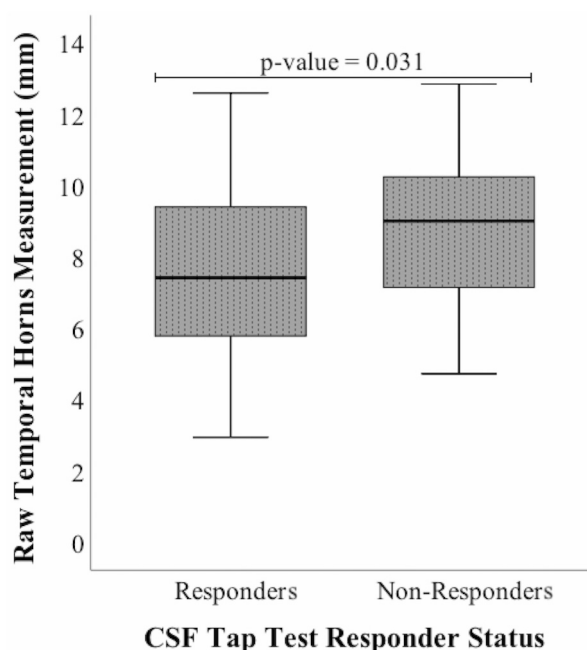
Smaller temporal horns (iNPH Radscale score and quantitative

**Table 2**  
Radiological characteristics of tap test responders and non-responders.

Variable	Tap Test Responders (n = 83)		Tap Test Non-Responders (n = 17)		p-value <sup>†</sup>
	Mean	SD	Mean	SD	
iNPH Radscale Total Score (0–12)	8.31	± 1.96	9.18	± 2.51	0.128
<i>iNPH Radscale Subitems</i>					
Evans Index (0–2)	1.99	± 0.11	2.00	± 0.00	0.651
Temporal Horns (0–2)	1.66	± 0.57	1.94	± 0.24	0.045*
Callosal Angle (0–2)	1.05	± 0.66	1.24	± 0.75	0.282
Narrow Sulci (0–2)	1.30	± 0.89	1.59	± 0.80	0.201
Sylvian Fissure (0–1)	0.71	± 0.46	0.71	± 0.47	0.967
Focally Enlarged Sulci (0–1)	0.83	± 0.38	0.71	± 0.47	0.232
Periventricular Hypodensity (0–2)	0.77	± 0.83	1.00	± 1.00	0.396

Abbreviations: SD: standard deviation.

<sup>†</sup> Statistically significant p-values are indicated with a \*.



**Fig. 1.** Comparison of Raw Temporal Horns Measurement between Tap Test Responders and Non-Responders.

measurement) are associated with a positive tap test responder status in iNPH patients. This result is in contradiction with previous reports showing that increased temporal horns predict positive outcomes after shunt surgery [22,23], as well as with studies showing that temporal horns cannot predict shunt outcome [24]. Virhammar's study [23] reported 13% smaller average temporal horns widths than our study, using a similar measuring method. Few explanations may contribute to these discrepancies. Patients in our sample are older than those reported in previous studies [22,23], suggesting a longer disease duration with more brain atrophy. Furthermore, the older age and wider temporal horns in our sample may reflect more comorbid Alzheimer's pathology [25], which could be linked with a poorer responder status. To test this hypothesis, a post-hoc evaluation of medial temporal lobe atrophy was carried out using Scheltens' scale. This analysis shows that the tap test responder group is below the threshold for Alzheimer's Disease ( $\geq 2$  for individuals aged 75–84) [21], while tap test non-responders are above. It should, however, be noted that Scheltens' scale has not been validated to distinguish patients with Alzheimer's disease from iNPH. Future studies should investigate the ability of the temporal horns subitem of the iNPH Radscale to distinguish temporal lobe atrophy from ventricular enlargement. Another explanation may be associated with the definition of responder status. Most prognostic studies define response to treatment as any improvement in locomotion, cognition or urinary symptoms. Here, we restricted the definition to any improvement in locomotion, as locomotion represents the key symptom of iNPH [26,27].

##### 4.3. The iNPH Radscale

The iNPH Radscale total score does not predict the CSF tap test responder status. This finding is supported by previous studies demonstrating that a combination of radiological parameters is unable to predict response to shunt surgery in iNPH [22,24,28,29]. The iNPH Radscale linearly correlates with iNPH symptom severity [7], indicating that more severe symptoms are associated with more severe radiological signs. However, it is well known that disease severity increases with disease duration [30], and a longer disease duration has a negative effect on shunting outcomes [27,31–33]. Consequently, more severe iNPH Radscale scores would be associated with worse treatment outcomes,

thus reducing the ability of the iNPH Radscale to predict the responder status. Furthermore, focusing on specific radiological signs rather than on composite scores, could uncover underlying comorbidities such as Alzheimer's pathology.

#### 4.4. TUG and CSF tap test

The CSF tap test is not a perfect proxy of a shunt, but TUG change after a tap test is a good predictor of shunt outcomes [10,11]. Previous studies have used a TUG improvement cut-off of  $\geq 10\%$  [10,11]. Meanwhile, false-negatives are a concern when using the tap test for predicting a positive shunt outcome [10,34,35]. We deliberately used a cut-off of 0% to maximise the sensitivity of the approach. Furthermore, a sensitivity analysis using different cut-offs for TUG improvement suggests a ceiling effect, as the association between smaller temporal scores and positive tap test responder status was not significant anymore at a cut-off of TUG improvement  $\geq 6\%$ . In addition, when separating the sample in clear responders (TUG improvement  $\geq 10\%$ ) and clear non-responders (TUG improvement  $< 0\%$ ), our results remained unchanged.

#### 4.5. Post-shunt outcome

Our post-shunt evaluations could not be used in this analysis because of the small size of the shunt non-responder sample ( $n = 4$ ), and because the outcome of the post-shunt evaluation was not standardised (i.e. TUG), but based on the subjective evaluation of the neurosurgeon during the post-shunt clinical evaluation.

#### 4.6. Strengths and weaknesses

The main strength of this study is the inclusion of a high number of iNPH patients with a quantitative locomotion measurement before and after the CSF tap test. Another strength relies on the use of a validated measure of locomotion (i.e. TUG) for defining tap test responder status in iNPH patients. However, the main limitation of the study is the absence of neuropathological confirmation for iNPH (and other comorbid neurological conditions) and the absence of standardised quantitative outcomes after shunt surgery.

## 5. Conclusion

The iNPH Radscale (total score) does not predict CSF tap test responder status, while a subitem of the iNPH Radscale – smaller temporal horns – is associated with locomotion improvement after CSF tap test. Future studies should verify these findings by including standardised post-shunt outcomes, and investigate the ability of the iNPH Radscale temporal horns width subitem to differentiate atrophy from ventricular enlargement without atrophy.

#### Data availability statement

Anonymised data that are not published in this article will be made available on request from any qualified investigator, after the approval by the Institutional Review Board of the Geneva University Hospitals.

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#### Disclosure of conflict of interest

The authors have no conflicts of interest.

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