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SHORT COMMUNICATION

Normal pressure hydrocephalus and cognitive impairment: The gait phenotype matters too

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Abstract

Background and purpose: Idiopathic normal pressure hydrocephalus (iNPH) is a chronic neurological disease resulting in progressive gait and cognitive disorders. We investigated whether the gait phenotype is associated with the severity of cognitive deficits in iNPH.

Methods: This retrospective study recruited 88 patients (mean age = 76.18 ± 7.21 years, 42% female). Patients were initially referred for suspicion of iNPH and underwent a comprehensive analysis, including gait analysis and cognitive evaluation.

Results: In this cohort (27% normal gait, 25% frontal gait, 16% parkinsonian gait, 27% other gait abnormalities), patients with parkinsonian and frontal gait had the lowest Mini-Mental State Examination (MMSE) scores and the slowest gait speed. Patients with normal gait had the highest MMSE scores and gait speed. Frontal gait was associated with lower MMSE score, even after adjusting for age, gender, comorbidities, white matter lesions, and education level ($\beta = -0.221$ [95% confidence interval (CI) = −3.718 to −0.150], $p = 0.034$). Normal gait was associated with the best MMSE scores, even after adjusting for the abovementioned variables ($\beta = 0.231$ [95% CI = 0.124–3.639], $p = 0.036$).

Conclusions: Gait phenotypes among iNPH patients are linked to global cognition as assessed with MMSE.

KEYWORDS
clinical evaluation, cognition, cognitive disorders, gait, normal pressure hydrocephalus

INTRODUCTION

Idiopathic normal pressure hydrocephalus (iNPH) is a chronic neurological condition resulting in progressive gait and cognitive disorders, irreversible if not diagnosed and treated early [1]. As the treatment consists of a neurosurgical intervention, correctly identifying suitable patients is crucial to avoid unnecessary invasive procedures. In this study, we focused on the gait phenotype to provide easily accessible information for clinicians in the evaluation of iNPH patients. We aimed investigated whether the gait

phenotype is associated with the severity of cognitive deficits in iNPH.

METHODS

This retrospective study recruited 88 patients (mean age = 76.18 ± 7.21 years, 42% female) from the Geneva iNPH protocol, according to prior study procedures [2]. In brief, patients were initially referred for suspicion of iNPH based on cognitive impairment, gait disorders, and/or urine incontinence; they underwent a standard diagnostic procedure, including gait analysis and Mini-Mental State Examination (MMSE) for the cognitive evaluation; a multidisciplinary board including behavioural neurologists, neuropsychologists, and physical therapists reviewed all data before a diagnosis of iNPH was made according to consensus American–European guidelines [1]. Inclusion criteria for this study were (i) a diagnosis of possible or probable iNPH, (ii) ability to walk without assistance, (iii) a video of gait evaluation, and (iv) MMSE evaluation. Exclusion criteria were any acute medical condition in the 3 months prior to evaluation and a secondary NPH. Two assessors (E.M., G.A.) evaluated gait phenotypes in video recordings and classified them as frontal gait, parkinsonian gait, normal gait, or other gait abnormalities, with a substantial agreement ($\kappa = 0.73$). Frontal gait consisted of short steps, a wide base of support, and a magnetic component (reduced step height), whereas parkinsonian gait consisted of short and/or shuffling steps, flexed posture, reduced arm swing, and normal base [3]; normal gait consisted of the absence of any clinical gait abnormalities, and other gait included all other neurological gait abnormalities (such as hemiparetic,

TABLE 1 Characteristics of the participants ($N = 88$).

Characteristic	Normal gait, $n = 28$	Frontal gait, $n = 22$	Parkinsonian gait, $n = 14$	Other gait, $n = 24$	p
Age, years	74.89 ± 7.94	77.04 ± 7.93	78.31 ± 5.70	76.45 ± 6.85	0.337
Female, *n* (%)	12 (23.5)	15 (29.4)	11 (21.6)	13 (25.5)	0.617
Disease duration, months	40.67 ± 63.01	39.10 ± 30.20	25.83 ± 19.95	40.84 ± 30.31	0.087
Comorbidity (GHS, 0–10)	1.47 ± 1.06	1.94 ± 1.15	2.00 ± 0.98	2.00 ± 1.11	0.117
Medication, *n*	3.71 ± 2.52	4.79 ± 2.24	4.79 ± 3.01	3.16 ± 3.38	0.332
MMSE (0–30)	26.19 ± 3.38	23.68[a] ± 4.29	22.54[a] ± 4.09	25.59 ± 3.44	0.002*
Education level, years	12.67 ± 3.12	11.00 ± 2.51	10.43 ± 4.73	11.69 ± 3.77	0.054
Risk factors					
Vascular (0–5)	1.33 ± 0.97	1.35 ± 1.02	1.29 ± 0.86	1.38 ± 1.04	0.993
Cardiovascular (0–4)	0.11 ± 0.32	0.42[b] ± 0.50	0.29 ± 0.62	0.22 ± 0.42	0.036*
Cerebrovascular (0–2)	0.06 ± 0.23	0.16 ± 0.37	0.08 ± 0.28	0.16 ± 0.45	0.529
White matter changes					
Frontal (0–6)	2.94 ± 1.67	3.03 ± 1.32	3.13 ± 1.62	2.35 ± 1.14	0.172
Parieto-occipital (0–6)	2.47 ± 1.87	2.74 ± 2.03	2.75 ± 1.89	2.48 ± 1.88	0.880
Temporal (0–6)	0.67 ± 1.10	0.97 ± 1.47	0.96 ± 1.23	0.74 ± 1.29	0.702
Basal ganglia (0–6)	0.39 ± 0.77	0.48 ± 0.93	0.54 ± 0.88	0.68 ± 1.05	0.651
Infratentorial (0–6)	0.22 ± 0.49	0.48 ± 0.96	0.42 ± 0.97	0.26 ± 0.58	0.830
Total score (0–30)	6.69 ± 4.94	7.71 ± 5.25	7.79 ± 4.61	6.52 ± 4.66	0.602
Gait speed, m/s	0.97 ± 0.17	0.62 ± 0.21[c]	0.58 ± 0.22[c]	0.79[c] ± 0.19	<0.001*
NPH scale					
Gait (0–4)	1.67 ± 0.59	2.16[d] ± 0.37	2.09[d] ± 0.52	1.97[d] ± 0.40	0.001*
Cognition (0–4)	1.86 ± 0.54	2.03 ± 0.66	2.14 ± 0.56	2.00 ± 0.67	0.292
Urinary (0–4)	0.97 ± 0.94	1.34 ± 1.01	1.05 ± 1.05	1.13 ± 0.94	0.481

Note: Results are given as mean ± SD, unless indicated otherwise.

Abbreviations: GHS, Global Health Status Scale; MMSE, Mini-Mental State Examination; NPH, normal pressure hydrocephalus.

[a]Patients with frontal gait and parkinsonian gait are significantly slower than patients with normal gait (respectively, $p = 0.006$ and $p = 0.001$); patients with parkinsonian gait are significantly slower than patients with other gait abnormalities ($p = 0.012$).

[b]Patients with frontal gait have significantly more cardiovascular risk factors than patients with normal gait ($p = 0.004$).

[c]Patients with normal gait are significantly faster than patients with frontal gait ($p < 0.001$), parkinsonian gait ($p < 0.001$), and other gait abnormalities ($p = 0.007$). Patients with other gait abnormalities are significantly faster than patients with frontal gait ($p = 0.002$) and parkinsonian gait ($p = 0.001$).

[d]Patients with normal gait have significantly lower scores than patients with frontal gait ($p < 0.001$), parkinsonian gait ($p = 0.003$), and other gait abnormalities ($p = 0.025$).

*Significant at $p < 0.05$.

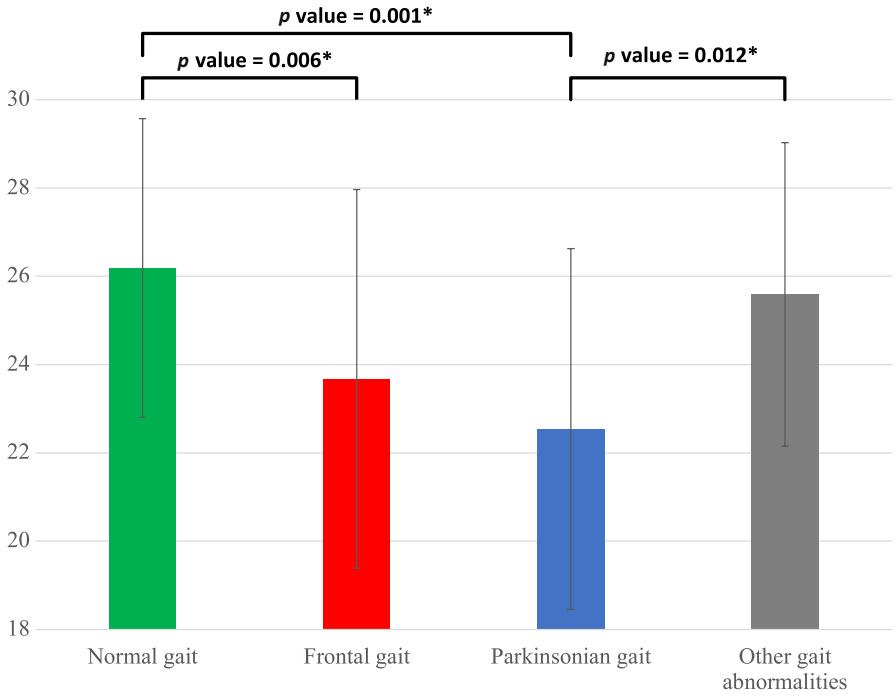

FIGURE 1 Mini-Mental State Examination and gait phenotypes. *Significance level was set at $p < 0.05$.

cerebellar, neuropathic, or mixed). Univariable linear regressions evaluated the relationship between MMSE score (dependent value) and each gait phenotype (independent value). Multivariable linear regressions were adjusted for age, gender, comorbidities, white matter changes, and education level. All statistical analyses were performed with SPSS version 23 (SPSS, Chicago, IL, USA). The ethical review board of the Geneva University Hospitals approved the study (Protocol 09-160R).

RESULTS

Clinical characteristics are presented in Table 1. The cohort consists of 27% patients with normal gait, 25% with frontal gait, 16% with parkinsonian gait, and 27% with other gait abnormalities. Patients with parkinsonian and frontal gait had both the lowest MMSE scores and the slowest gait speed compared to patients with normal gait or other gait abnormalities (Figure 1). Patients with normal gait had the highest MMSE scores and gait speed. Frontal gait was significantly associated with lowest MMSE score, even after adjusting for age, gender, comorbidities, white matter lesions, and education level (β = −0.221 [95% confidence interval (CI) = −3.718 to −0.150], $p = 0.034$). Normal gait was associated with the best MMSE scores, even after adjusting on the above-mentioned variables ($\beta = 0.231$ [95% CI = 0.124–3.639], $p = 0.036$). Parkinsonian gait tended to be associated with lower MMSE scores, but this association was not significant after adjustment (β = −0.146 [95% CI = −3.655 to 0.636], $p = 0.165$). Other gait abnormalities showed no association with MMSE score ($\beta = 0.120$ [95% CI = −0.754 to 2.825], $p = 0.253$).

DISCUSSION

This study found a significant association between gait phenotypes and global cognition assessed with MMSE in iNPH patients. Frontal gait was associated with the lowest MMSE scores and normal gait with the highest MMSE scores.

This association between cognition and gait in iNPH is controversial in the literature. A previous study found an association between gait severity and several specific neuropsychological tests [4], which points toward a common pathophysiological mechanism. Our results support a link between gait disorder and global cognition in iNPH, more specifically, that frontal gait is associated with poor cognition. This is particularly relevant, because global cognition measured with MMSE is the best predictor for cognitive improvement after neurosurgical intervention [5] and frontal gait represents the clinical gait feature that improved the most after cerebrospinal fluid tapping [2]. Stratifying patients according to their gait phenotype might help clinicians to identify good candidates for surgical treatment, especially when considering that iNPH patients with poor cognition are less responsive than those with normal cognition, except for those with apathy [6].

A major limitation of our study is the lack of cognitive evaluation after neurosurgical intervention to evaluate whether the gait phenotype may also be a suitable predictor of cognitive improvement. This study focuses on the interest of gait phenotype evaluation for clinicians in their daily practice. We must emphasize that assessment of gait phenotype alone is not sufficient in the management of iNPH and should be integrated into a holistic evaluation, especially as age-related comorbidities may mimic or contribute to iNPH symptoms. We would therefore recommend that future prospective studies

include not only the evaluation of quantitative gait parameters but also the evaluation of gait phenotype.

In conclusion, our study showed that gait phenotypes among iNPH patients are linked to global cognition as assessed with MMSE. This reinforces that gait phenotype represents a useful clinical tool for the first-line evaluation of iNPH patients.

AUTHOR CONTRIBUTIONS

Eric Morel: Conceptualization (lead); formal analysis; investigation; methodology; writing–original draft preparation. **Alma Lingenberg:** Investigation; writing–review & editing. **Stéphane Armand:** Investigation; resources; writing–review & editing. **Frédéric Assal:** Conceptualization (supporting); writing–review & editing. **Gilles Allali:** Conceptualization (lead); formal analysis; funding acquisition; methodology; supervision; writing–review & editing.

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CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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