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A combined cognitive and gait quantification to identify normal pressure hydrocephalus from its mimics: The Geneva's protocol

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ABSTRACT

Objectives: Idiopathic normal pressure hydrocephalus (iNPH) is very prevalent in aging, underdiagnosed, and represents a rare cause of reversible neurological condition. The clinical triad of iNPH – gait, cognitive and urinary symptoms – and its neuroradiological features (i.e. ventriculomegaly) are not specific and found a various neurodegenerative and/or vascular conditions. We present our iNPH standardized protocol at the Geneva University Hospitals involving a multispecialty team of behavioral neurologists, neurosurgeons, neuropsychologists, engineers, and physical therapists. Based on a pragmatic approach, the goal of this protocol is to improve the identification of older patients with iNPH from its mimics (i.e. vascular dementia or other parkinsonian syndromes).

Patients and methods: We used a novel standardized paradigm with a simultaneous quantification of cognition and gait (dual task gait assessment and mental imagery of locomotion) before and 24 h after CSF tapping.

Results: We assessed 125 patients with suspicion of iNPH (age: 75.9 ± 7.4 years; 34.4% female) in 5 years: 54.4% of probable/possible iNPH and 45.6% of mimics. Among the mimics, vascular dementia (24.6%) and patients with multifactorial conditions (19.9%) were the two most common diagnoses. A total of 27 patients with iNPH (39.7%) accepted the neurosurgical shunt procedure.

Conclusion: This report shows that a quantified gait and cognitive assessment – using dual-task paradigms – before and after CSF tapping is feasible among older adults with suspicion of iNPH and that this multidisciplinary approach contributes to the identification of patients with iNPH from its mimics.

1. Introduction

Idiopathic normal pressure hydrocephalus (iNPH) was first described by Salomon Hakim in Bogota in 1957 [1,2] and represents a prevalent neurological conditions in older adults reaching 6% after 80 years [3]. A classic triad of clinical symptoms associating gait, cognitive and urinary disturbances with disproportional ventricular enlargement at brain imaging constitute this reversible condition [4]. Unfortunately, these clinical signs are unspecific and found in various frequent neurological conditions, such as vascular dementia or Alzheimer's disease with comorbid urinary problems (i.e. iNPH mimics). Moreover, patients with iNPH and mimics present similar gait and cognitive profiles [5,6]. Hence, identifying iNPH patients from its mimics represents a real challenge for clinicians [7].

Herein, we developed a novel and original protocol using a quantified assessment of gait parameters and cognitive measures using the dual task paradigm performed before and 24 h after the CSF tap test. Furthermore, to better assess the higher level of gait control, we included a validated mental imagery task of locomotion: the imagined Timed up and go [8]. Here, we describe our five-year experience of patients with suspicion of iNPH at the Division of Neurology of the Geneva University Hospitals involving a multispecialty team of behavioral neurologists, neurosurgeons, neuropsychologists, engineers, and physical therapists. Establishing the feasibility of a clinical protocol that aims to identify older adults with iNPH from its mimics will improve the standard of care of older adults with gait and cognitive decline that are both prevalent in aging, and help to better decide which patients should benefit from a ventricular shunt or iterative CSF tap test.

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2. Patients and methods

2.1. Staffing

The Geneva's protocol staff includes two behavioral neurologists, one resident in neurology, one neurosurgeon, two neuropsychologists, one physical therapist and one engineer in movement science.

2.2. Pre-visit assessment

Patients are referred by neurologists (92%), geriatricians (4.8%), or neurosurgeons (4.2%). Prior to their assessment, the patient's medical chart is reviewed by a behavioral neurologist to screen the feasibility of the protocol on an outpatient basis including brain imaging assessment (MRI in 88% or CT-scans in 12% were performed on an outpatient basis in all patients prior to our assessment), review of the medication with a special attention to anticoagulant drug that would contraindicate CSF tap test procedure.

2.3. iNPH clinic assessments (Fig. 1)

The iNPH clinic assessment is conducted on two consecutive days in or outpatient clinic. During the first day (7 h: from 8:00 am to 3:00 pm), the patients first perform a blood screen that includes a complete blood count, prothrombin time and partial thromboplastin time, electrolytes, and renal and liver function tests, folate/B12 deficiency, thyoïd, and syphilis, Lyme and HIV serologies. Then, patients go through a quantitative gait assessment, a neuropsychological test battery, a comprehensive neurological examination, and the CSF tap test is collected. Two hours after the CSF tap test, patients can leave the outpatient clinic and come back the day after for the post-CSF tap test assessment. During the second day − post-CSF tap test assessment (2 h: from 8:00 am to 10:00 am), patients perform a quantitative gait assessment and a neuropsychological assessment focusing on cognitive functions usually disturbed in iNPH (i.e. attention, executive function, manual dexterity and callosal transfer).

2.4. Gait assessment

The gait assessment consists on a quantitative spatio-temporal gait evaluation at comfortable walking speed performed in ecological condition, while patients wearing their own shoes, as previously described [5,9]. Five individual randomized conditions are performed: usual walking and walking while performing four different dual tasks: forward counting from 1; backward counting from 50; phonemic verbal fluency (enumerating words starting by letter p); and categorical verbal fluency (generating animals' name). A standardized instruction for the dual tasks is given by the physical therapist: to walk and to perform the cognitive task at the best of their capacity without prioritization. Mean value and coefficient of variability of spatiotemporal gait parameters (that include walking speed, stride time, stride width and heel height) are computed based on the measurement of the heel marker trajectories on a distance of 10 m with an optoelectronic system including 12 cameras. The coefficient of variability (CV) is computed with the following formula: CV (%) = (standard deviation of gait parameter/mean value of gait parameter) * 100. For the mental imagery task of locomotion, we are using the imagined version of the Timed up and go (TUG) [8]: participants are asked to perform the TUG at their self-selected normal speed. After completing the TUG, the physical therapist asks the patient to imagine the TUG while sitting in a chair. Participants can choose to do the imagined TUG with their eyes opened or closed, and they are not instructed on the modality of mental imagery (kinaesthetic versus visual mental imagery modality). The gait assessment is conducted pre-CSF tap test and 24 h after CSF tap test, as it can be evaluated anytime in the first 24 h after CST tap test [10]. Both gait evaluations take around 45 min each.

2.5. Neuropsychological assessment

A standardized neuropsychological assessment is conducted with each participant before and 24 h after CSF tap test, as previously described [6]. The pre-CSF tapping assessment includes a detailed evaluation of executive functions (Color Trails test [11], Stroop test [12], phonemic and categorical verbal fluencies [13]), attention (Wechsler Adult Intelligence Scale − III symbol digit test and digit span [14]; Wechsler Memory Scale − III spatial span [15]), memory (the French version of the Free and Cued Selective Reminding Test [16]), callosal transfer (verbal dichotic listening), manual dexterity (Purdue pegboard test [17]), and language (confrontation naming pictures: Test de dénomination orale de 80 images [18]). The other cognitive domains are clinically evaluated: visuo-spatial recognition with the overlapping figures, illusory contours and identification of a complex figure; ideomotor praxis with the execution of meaningful gestures, pantomime tool use and imitation of hand gestures; visuo-constructive skills with the copy of 2-D and 3-D figures. Global cognitive functioning is assessed with the Mini-Mental State Examination [19]. Among the neuropsychiatric domains, depression and anxiety are assessed with the hospital anxiety and depression scale [20], and apathy with the Starkstein apathy scale [21]. Then, the post CSF tapping assessment conducted 24 h after CSF tap test focuses on executive function, attention, manual dexterity and callosal transfer. The pre-CSF neuropsychological evaluation takes around 2 h and the post-CSF 1 h.

2.6. CSF tap test

The CSF tap test consists on the removal of 40 ml of CSF using a 20-gauge spinal needle in lateral supine position. The opening pressure is measured with a manometer. CSF cells count, differential cell count, protein concentration and immunofixation electrophoresis are routinely measured. And, when the patients agree, we also include a measurement of CSF total tau, phospho-tau and Aβ42 proteins.

2.7. Post iNPH clinic assessments

A diagnosis is assigned after reviewing all pre-CSF tap test clinical and neuropsychological information as well as brain imaging and blood/CSF tests in a consensus case conference involving behavioral neurologists and neuropsychologists. A diagnosis of iNPH is based on the iNPH international consensus guideline criteria [22], including clinical criteria and Evan's index > 0.3 whereas alternate diagnoses followed standard international criteria. Importantly, iNPH criteria do not include comparisons between pre and post CSF assessments [22]. If clinically relevant, other ancillary tests, such as DAT-Scan or PET-Scan, were suggested by the participants of the consensus case conference, and are conducted outside the protocol. The flow of the patients from initial referral to shunt surgery is presented in Fig. 2.

2.8. Clinical covariates

As comorbidity and vascular risk factors are highly prevalent in iNPH patients and represent both major issues in iNPH [7,23], we quantified them with validated scales: the Global health status score (GHS; range 0–10) for diabetes, chronic heart failure, arthritis, hypertension, depression, stroke, Parkinson's disease, chronic obstructive pulmonary disease, angina, and myocardial infarction [24], the vascular risk factor score (range 0–5) for the presence of diabetes, hypertension, hypercholesterolemia, body mass index > 30 or smoking, the cardiovascular risk factor score (range 0–4) for the presence of myocardial infarction, angina, arrhythmia or chronic heart failure, and the cerebrovascular score (range 0–2) for the presence of stroke or transient ischemic attacks [25]. We used the validated iNPH grading scale [26] for quantifying iNPH severity. Finally, white matter changes on CT or MRI are quantified with the age-related white matters changes