Review paper

Psychometric hepatic encephalopathy score (PHES) – when, how, why, and why not: a guide for the unfamiliar

Nikola Mumdzhiev, Rumen V. Tenev, Mariana P. Radicheva

Gastroenterology Department, UMHAT "Prof. Stoyan Kirkovitch", Stara Zagora, Bulgaria

Gastroenterology Rev 2025; 20 (1): 31–35
DOI: https://doi.org/10.5114/pg.2024.145382

Key words: portosystemic hepatic encephalopathy score, minimal hepatic encephalopathy.

Address for correspondence: Nikola Mumdzhiev, Gastroenterology Department, UMHAT Prof. Stoyan Kirkovitch, Stoletov 2 Boulevard, Stara Zagora 6000, Bulgaria, e-mail: niko_mu2002@yahoo.com

Abstract

Psychometric hepatic encephalopathy score (PHES) has established itself as one of the most used tests for detecting minimal hepatic encephalopathy. To use it in a certain population one needs to determine what the norms are, and have a proper set of inclusion and especially exclusion criteria. When performing the test (either for validating or as a search tool) authors may benefit from a little guidance. All the 5 tests – DST (Digital Symbol test), Number Connection Test A (NCT A), Number Connection Test B (NCT B), Serial Dotting Test (SDT), Line Drawing Test (LDT) – have certain parameters to follow. In time, deviations have appeared, and comparability between different samples has become somehow limited. As new tests are emerging, and in order to compare, one must be familiar with the tests' variants, benefits, and limitations.

Introduction

Liver cirrhosis, similar to heart failure or kidney failure, incorporates irreversible advanced organ damage due to multiple aetiologies – most often viral (hepatitis B, C, or D) and toxic (alcohol), but also autoimmune (autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis), metabolic (metabolic associated fatty lived disease, Wilson disease, and haemochromatosis) and rarely nowadays cryptogenic. In the natural development of cirrhosis, two phases are distinguished: the asymptomatic compensated phase, and the clinically apparent decompensated phase. The last is determined by the development of jaundice, ascites, bleeding, or encephalopathy [1]. Hepatic encephalopathy (HE) is one of the most damaging forms of decompensation both for the patients' lifestyle and their health prognosis, but also for their caregivers and family [2]. Its importance is signified in the most used scale: the Child-Pugh score [3]. The EASL/AASL 2014 Guidelines on Hepatic encephalopathy brought much needed classifications and definitions regarding hepatic encephalopathy, including and acknowledging the West Haven classification [4]. In it, the most subtle mentality changes, named covert hepatic encephalopathy by the ISHEN classification [5], are divided into minimal hepatic encephalopathy (MHE) and stage 1 hepatic encephalopathy. MHE is determined only by alterations in psychometric and neurophysiologic tests [6]. From all available, the portosystemic hepatic encephalopathy score (PHES) is widely accepted and has been validated in several countries (Table I). It can be obtained from Hannover Medical School (Hannover, Germany), which holds the copyright (Weissenborn.karin@mh-hannover.de). Guides for the appropriate management of the PHES test are readily available. Nevertheless, there are differences in the standardisation methodology used by different researchers (both when managing the tests of the battery or their results) making international comparison troublesome. Despite its positive sides, PHES has its pitfalls, and ISHEN encourages the use of 2 different tests when performing clinical trials [5].

When to perform PHES

In clinical practice all cirrhotic patients should be tested for MHE [7]. It determines disease prognosis and predicts quality of life, and the results help guide

Table I. Countries that have validated the PHES, the number of healthy participants, the respective year of validation, and references

Year	Country	Healthy participants	Reference
2001	Germany	120	
2006	Spain	884	[13]
2008	Italy	228	[11]
2008	United Kingdom	526	
2010	India	83	[12]
2011	Mexico	743	[14]
2011	Portugal	115	
2012	South Korea	200	[22]
2013	China	146	
2013	Poland	316	[17]
2015	China	843	
2016	USA	308	[20]
2016	Romania	260	[18]
2016	Cuba	520	[15]
2017	Turkey	185	[23]
2017	Korea	315	
2020	France	196	[24]
2021	Cameroon	102	[19]
2023	Thailand	194	[16]

caregivers and family. Unfortunately, testing for minimal hepatic encephalopathy is limited to clinical trials or studies, because the tests are time consuming or require specific education or machinery. Furthermore, the cost effectiveness of treating a large population of clinically healthy individuals based on changes in psychometric results remains questionable [8].

When PHES is being performed (used, validated, or standardised) several inclusion and exclusion criteria must be met. Also, the test needs to be standardised for the population tested (i.e. German norms are applicable in Germany and should not be used anywhere else). Table I summarises the countries in which PHES has been standardised. The exclusion criteria are as follows: history or a present episode of overt hepatic encephalopathy; oncologic diseases, especially primary hepatic tumours; TIPS or portosystemic shunt surgery; an episode of gastrointestinal bleeding or spontaneous bacterial peritonitis in the last 3 months; excessive alcohol intake; medications used for treatment of hepatic encephalopathy; neurological or psychiatric conditions or medication; severe respiratory, cardiac, or kidney injuries; uncorrected vision impairment; and illiteracy. Most of these are straightforward and self-explanatory because they either directly change the subject's mental capacity or exacerbate or treat hepatic encephalopathy.

Grading hepatic encephalopathy is a specific task requiring deep understanding of the criteria in the West Haven classification (WHC) [4]. Differentiating between covert and overt hepatic encephalopathy (setting the border between Stage I and Stage II in the WHC) is easy when using signs such as asterixis or disorientation for time [9]. Diagnosing grade 1 hepatic encephalopathy, on the other hand, relies on subjective tools, the best of which is dyscalculia – impairment of addition and especially subtraction (usually the task is to subtract 7 from a number such as 36). Such subtle clinical findings perfectly fit the spectrum of HE, between marked and clinically unimpaired, but are with low reliability and reproducibility.

How to perform PHES

The PHES test was developed in the early 1980s as the PSE syndrome test by the neuropsychologist Wolfgang Hamster and the gastroenterologist Hans Schomerus. After initial assessment of more than 20 tests [10] 3 stood out: the digit symbol test (DST), the line tracing test (LTT), and the serial dotting test (SDT). To those 3 the number connection tests (NCT) A and B were added because they were the most frequently used up to that point of time. These 5 tests (DST, NCT A and B, SDT, and LTT) form the PHES battery. It is a tool able to discover MHE – alterations of attention, visuo-spatial perception, and psychomotor function in patients with liver cirrhosis.

When performing PHES, the availability of a quiet room is mandatory; the active time of the day and a pattern for the explanation of the test should be used. The use of a pencil is preferred. The age and education (and in some cases the gender) of the test subject should be noted because these parameters are of statistical significance to performance.

DST (digital symbol test) – a table is shown to the patient, in which a number corresponds to a specific symbol. After a trial run, the patient is asked to fill up as many corresponding symbols in an empty table consisting of 80 numbers. The test subject has 90 s at their disposal and must not skip matching pairs. The final score is the number of correct corresponding symbols. In some instances, 2 min and not 90 s are used, rendering the results of the 2 variants incomparable.

Number connection test A (NCT A) - the test consists of 25 scattered circles numbered from 1 to 25. After a trial run, the patient is asked to connect without any mistakes the circles from 1 to 25 as fast as possible. If a mistake occurs, the patient must stop, correct the

mistake, and continue while the time is still measured. The final score is the time (in seconds) needed to complete the task.

It is important to note that the size of the circles or the numbers, or their distribution on the sheet of paper are, in some authors' versions, different to the original scale [11]. This difference could be of importance when comparing the results of different authors (different NCT-A) because size and spatial distribution could affect the test subject's speed.

Number connection test B (NCT B) – the test consists of 13 numbers and the first 12 letters from the alphabet of the patient's native language. After a trial run, the patient is asked to connect the circles in a succession patter "1 – A – 2 – B and so on up to 13". If a mistake occurs the patient must stop, correct the mistake, and continue while the time is still measured. The final score is the time (in seconds) needed to complete the task.

As in NCT-A, the size of the circles, letters, numbers, and their distribution could affect performance. The use of letters demands test subjects who have an education. In populations with high rate of illiteracy this could prove troublesome. The use of specific figures instead of letters was performed in an Indian group [12]. Although useful, this change alters the test. Different cognitive functions are used when following letters, compared to when following a figure pattern.

Having a test with letters in an unfamiliar language urges all authors to provide their versions of the NCT-B using a suitable alphabet. Size and position should be maintained.

Serial dotting test (SDT) – the test consists of 100 circles, in which, after an initial trial run, the test subject must place a central dot as fast as possible. The final score is the time (in seconds) needed to complete the task.

Line drawing test (LDT) – the test consists of a maze formed from 2 parallel lines. The patient must draw a line into the maze without touching or crossing the walls of the maze. Two results are measured – the time taken to complete the maze (in seconds) and the number of errors.

Although complimentary, the 2 results differ in the cognitive functions they measure. It was found that the number of errors is more discriminative than the performance time when searching for MHE. Nevertheless, in many studies a sum score is used [13–16]. In the Italian version of the study a specific formula named "error-weighted time" was introduced [11] and used by many thereafter [17–19]. The combining of the 2 results changes the range of the PHES and makes inter-study comparison troublesome. When doing so, one must use raw data (not easily assessable) to provide LTT-sum score or LTT-error-weighted-time score. Some authors [18] even transform their own data in all the variants in order to achieve comparison [18].

Calculating the number of errors also shows discrepancies. In the original a transparent scheme is used. It overlaps the maze and divides it into segments. For each segment error points are designated (0 – into the maze, 1 – touching the border of the maze, 2 – outside the maze, 3 – outside the overlapping scheme). There are 365 segments and therefore a maximum error score of 1095. Some authors use a simplified version without an overlapping scheme (0 – into the maze, 1 – touching the border of the maze, 2 – outside the maze) giving points for each error, with no maximum error score. [16] Such evaluation differences provide additional discordance between studies.

Why PHES (advantages of PHES)

Several distinctive features make PHES the preferred test to diagnose minimal hepatic encephalopathy. High sensitivity and specificity are important for every evaluation tool. In this case we can add simplicity and low cost. Neither is true for the neurophysiological tests, where specific, often expensive, equipment is needed. In the case of EEG, the evaluator also needs specific training. PHES is easily applicable, with no sophisticated education needed, up to the point where middle medical personnel (trained nurses) can effortlessly perform it. Availability, due to the efforts of Prof. Weissenborn and the Hanover Medical University, plays a role when starting the endeavour of searching for MHE. That is why the number of countries where it has been validated, and is used, continues to grow. In real practice it is the most used test for MHE, and in some countries online calculators have been introduced (i.e. in Spain: http://www.redeh.org/phesapp/datosE.html). The EASL/AASLD guideline [4] recommends using at least 2 tests to detect MHE in clinical trials. Usually, PHES is one of them, deemed the "gold standard" by many. There are also trials where PHES alone proves non-inferior to the "2 test" rule [20].

Why not PHES (disadvantages of PHES)

The most prominent limitation of PHES, which is an obstacle for all psychometric tests, is the need for standardisation. The tests should be standardised for each nation. Effects of age and education must also be considered, as well as occupation and gender in some cases. As mentality changes with generations, some authors even suggest re-evaluation of the normal data after periods of time within a distinct population [21].

As per exclusion criteria, illiterate people cannot be tested because NCT-B requires knowledge of the alphabet. Changing NCT-B using symbols [12], as mentioned above, tests different cognitive functions.

In some studies [11], a practice effect has been observed. It is seen when readministering PHES even after long periods of time. This may limit the test's practical value, rendering it applicable only when discovering MHE, but useless for follow-up or determining a medication's effect.

A bedside test is easily performed but still needs direct contact with the test subjects. Newer tests, like the animal naming test, can be performed via a simple phone call while the patient is at home. For that reason, the latter have received a special attention in the latest guidelines [7].

Conclusions

There is no "gold standard" for detecting minimal hepatic encephalopathy. Nevertheless, PHES is the most used and easily applied test. With increased utilisation, variations of the PHES have appeared. It will be useful to have strict rules with comprehensive instructions for administering the test, as well as for evaluating it.

Funding

No external funding.

Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

References

1. D'Amico G. The clinical course of cirrhosis. Population based studies and the need of personalized medicine. J Hepatol 2014; 60: 241-2.
2. Rakoski MO, McCammon RJ, Piette JD, et al. Burden of cirrhosis on older Americans and their families: analysis of the health and retirement study. Hepatology 2012; 55: 184-91.
3. Bustamante J, Rimola A, Ventura PJ, et al. Prognostic significance of hepatic encephalopathy in patients with cirrhosis. J Hepatol 1999; 30: 890-5.
4. Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatology 2014; 60: 715-35.
5. Bajaj JS, Mullen KD, Amodio P, et al. Review article: the design of clinical trials in hepatic encephalopathy: an International Society for Hepatic Encephalopathy and Nitrogen Metabolism (ISHEN) consensus statement. Aliment Pharmacol Ther 2011; 33: 739-47.
6. Weissenborn K, Ennen JC, Schomerus H, et al. Neuropsychological characterization of hepatic encephalopathy. J Hepatol 2001; 34: 768-73.
7. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the Study of the Liver EASL Clinical Practice Guidelines on the management of hepatic encephalopathy. J Hepatol 2022; 77: 807-24.
8. Bajaj JS, Pinkerton SD, Sanyal AJ, Heuman DM. Diagnosis and treatment of minimal hepatic encephalopathy to prevent motor vehicle accidents: a cost-effectiveness analysis. Hepatology 2012; 55: 1164-71.
9. Bajaj JS, Wade JB, Sanyal AJ. Spectrum of neurocognitive impairment in cirrhosis: implications for the assessment of hepatic encephalopathy. Hepatology 2009; 50: 2014-21.
10. Schomerus H, Hamster W. Neuropsychological aspects of portal-systemic encephalopathy. Metab Brain Dis 1998; 13: 361-77.
11. Amodio P, Campagna F, Olianas S, et al. Detection of minimal hepatic encephalopathy: normalization and optimization of the Psychometric Hepatic Encephalopathy Score. A neuropsychological and quantified EEG study. J Hepatol 2008; 49: 346-53.
12. Dhiman RK, Kurmi R, Thumburu KK, et al. Diagnosis and prognostic significance of minimal hepatic encephalopathy in patients with cirrhosis of liver. Dig Dis Sci 2010; 55: 2381-90.
13. Romero Gómez M, Cordoba J, Jover R, et al. Normality tables in the Spanish population for psychometric tests used in the diagnosis of minimal hepatic encephalopathy. Med Clin (Barc) 2006; 127: 246-9.
14. Duarte-Rojo A, Estradas J, Hernandez-Ramos R, et al. Validation of the psychometric hepatic encephalopathy score (PHES) for identifying patients with minimal hepatic encephalopathy. Dig Dis Sci 2011; 56: 3014-23.
15. Ruiz MAP. Normality tables of the population in Cuba for the psychometric tests used in the diagnosis of minimal hepatic encephalopathy. Rev Gastroenterol Peru 2016; 36: 29-34.
16. Thanapirom K, Wongwandee M, Suksawatamnuay S, et al. Psychometric hepatic encephalopathy score for the diagnosis of minimal hepatic encephalopathy in thai cirrhotic patients. J Clin Med 2023; 12:
17. Wunsch E, Koziarska D, Kotarska K, et al. Normalization of the psychometric hepatic encephalopathy score in Polish population. A prospective, quantified electroencephalography study. Liver Int 2013; 33: 1332-40.
18. Badea MA, Drug VL, Dranga M, et al. Diagnosis of minimal hepatic encephalopathy in a tertiary care center from eastern Romania: validation of the psychometric hepatic encephalopathy score (PHES). Metab Brain Dis 2016; 31: 1463-71.
19. Djomatcho LP, Kowo MP, Ndam AN, et al. Normalisation of the psychometric encephalopathy score within the Cameroonian population. BMC Gastroenterol 2021; 21: 287.
20. Duarte-Rojo A, Allampati S, Thacker LR, et al. Diagnosis of covert hepatic encephalopathy: a multi-center study testing the utility of single versus combined testing. Metab Brain Dis 2019; 34: 289-95.
21. Weissenborn K. PHES: one label, different goods?! J Hepatol 2008; 49: 308-12.

22. Seo YS, Yim SY, Jung JY, et al. Psychometric hepatic encephalopathy score for the detection of minimal hepatic encephalopathy in Korean patients with liver cirrhosis. J Gastroenterol Hepatol 2012; 27: 1695-704.
23. Özbaş B, Keskin O, Hecker H, et al. Determination of Turkish norms of psychometric tests for diagnosing minimal hepatic encephalopathy and proposal of a high sensitive screening test battery. Hepatol Int 2021; 15: 1442-55.
24. Coubard OA, Ober KM, Gaumet M, et al. Standardization of the psychometric hepatic encephalopathy score in a French population. PLoS One 2021; 16: e0257136.

Received: 6.01.2024
Accepted: 27.04.2024
Online publication: 2.12.2024