

QuickStroop for screening for minimal hepatic encephalopathy in patients with cirrhosis

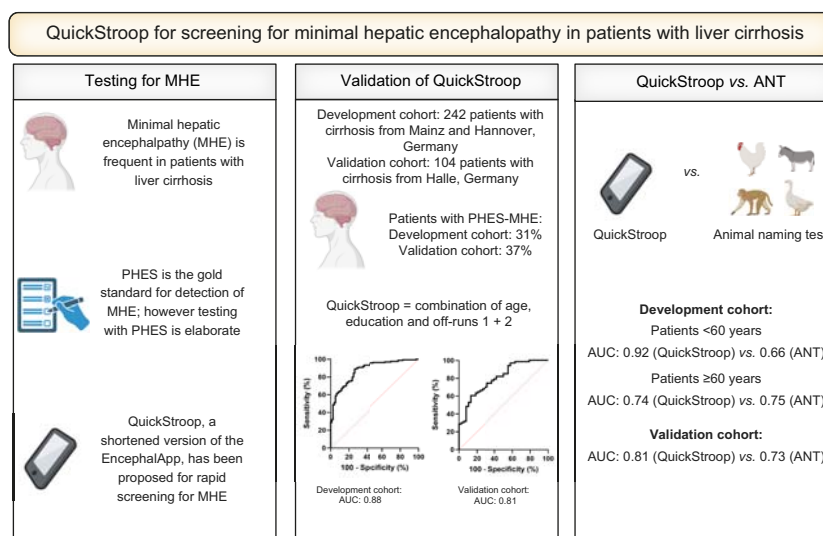
Authors

Christian Labenz, Simon J. Gairing, Leonard Kaps, ..., Cristina Ripoll, Robin Greinert, Benjamin Maasoumy

Correspondence

Christian.labenz@unimedizin-mainz.de (C. Labenz).

Graphical abstract



Highlights:

- QuickStroop, a shortened version of the Stroop EncephalApp, has recently been proposed for screening for MHE.
- QuickStroop had a good discriminative ability to detect MHE in patients aged <60 but was suboptimal in patients aged >60.
- The discriminative ability of QuickStroop to detect MHE appears to be superior to the ANT.
- QuickStroop only takes 34.5 s to complete.

Impact and implications:

QuickStroop, a shortened version of the Stroop EncephalApp, has recently been proposed for screening for MHE in patients with cirrhosis in the USA. In this study, we validated QuickStroop for patients in Germany with cirrhosis and demonstrate a good diagnostic accuracy for detecting MHE, especially in patients below 60 years of age. Additionally, QuickStroop might be superior to the ANT in patients below 60 years of age. The use of QuickStroop in clinical practice could facilitate screening for MHE.

QuickStroop for screening for minimal hepatic encephalopathy in patients with cirrhosis

Christian Labenz^{1,2,*}, Simon J. Gairing^{1,2}, Leonard Kaps^{1,2}, Alena F. Ehrenbauer³, Eva M. Schleicher^{1,2}, Sophie Mengel^{1,2}, Julius F.M. Egge³, Maria M. Gabriel⁴, Peter R. Galle^{1,2}, Heiner Wedemeyer³, Alexander Zipprich^{5,6}, Cristina Ripoll^{5,6}, Robin Greinert^{5,†}, Benjamin Maasoumy^{3,†}

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Background & Aims: QuickStroop, a shortened version of the Stroop EncephalApp, has recently been proposed for screening for minimal hepatic encephalopathy (MHE) in patients with cirrhosis in the USA. At present, there are no data on its clinical utility for MHE screening in patients in Europe, and only limited data are available regarding its comparison to the Animal Naming Test (ANT).

Methods: In total, 242 patients with cirrhosis without signs of hepatic encephalopathy (HE) \geq grade 1 and no history of overt HE were included as the development cohort. Another independent cohort comprising 104 patients with cirrhosis from a different center served as a validation set. MHE was defined using the psychometric hepatic encephalopathy score (PHES) (PHES-MHE). All patients were tested with the complete EncephalApp Stroop. A subset was also tested with the ANT. Regression formulas were fitted for patients above and below the age of 60 years, including the first two off-state runs, age, and school education (QuickStroop).

Results: PHES-MHE was detected in 76 (31%) patients. The first two off-state runs of the EncephalApp demonstrated a comparable discriminative ability to the complete Stroop test in distinguishing between patients with and without PHES-MHE. QuickStroop had a better discriminative ability in patients below than above the age of 60 years. The discriminative ability of QuickStroop (total cohort: AUC 0.88) was superior to ANT (AUC 0.70). QuickStroop predicted PHES-MHE with a sensitivity of 74% and a specificity of 89%, and took a median of only 34.5 s to complete. The acceptable discriminative ability of QuickStroop was confirmed in the validation cohort (AUC 0.81).

Conclusion: QuickStroop is a rapid screening tool to identify patients at risk for PHES-MHE, especially in patients below 60 years of age.

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Introduction

Hepatic encephalopathy (HE) is a severe complication of patients with liver cirrhosis with an increasing incidence in the Western world.^{1,2} Minimal HE (MHE) is the lowest grade of HE and can only be detected by using specialized tests.³ Although below the clinical detection level, MHE has a significant impact on the daily life of patients. MHE affects quality of life, is associated with car crashes, falls, a higher risk of overt HE (OHE) and even poorer survival.^{4–7} Therefore, detection in clinical practice and subsequent initiation of potential treatment would both be desirable.

Currently, the gold standard for detection of MHE is the psychometric hepatic encephalopathy score (PHES).³ Although readily available with country-specific norms, testing for MHE with PHES is routinely neglected by physicians mostly because of time restrictions.^{8,9} However, testing for

MHE appears to be mandatory for managing patients with cirrhosis, given that its prevalence ranges between 25% and 50% and it has detrimental effects on affected patients.¹⁰ Recently, QuickStroop, a shortened version of the Stroop EncephalApp, was introduced for predicting PHES-MHE.¹¹ Given that QuickStroop only takes ~30–60 s, it could be easily implementable into outpatient visits of patients with cirrhosis. However, external validations of QuickStroop and country-specific cut-offs to predict the presence of PHES-MHE are mostly lacking. In addition, the performance of QuickStroop compared with other readily available rapid screening tests for predicting PHES-MHE, such as the Animal Naming Test (ANT), are scarce.¹² Therefore, this study evaluated QuickStroop in patients with liver cirrhosis in Germany and determined cut-offs according to the Youden's index as well as with at least 90% sensitivity for PHES-MHE. Additionally, we

* Corresponding author. Address: Department of Internal Medicine I, University Medical Center of the Johannes Gutenberg-University, Langenbeckstrasse 1, 55131 Mainz, Germany. Tel: +49 6131 17 2380; Fax: +49 6131 17 477282.

E-mail address: Christian.labenz@unimedizin-mainz.de (C. Labenz).

† These authors share senior authorship.

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compared the diagnostic accuracy of QuickStroop with the ANT.

Materials and methods

Patient cohorts

For this analysis, 254 patients with cirrhosis were prospectively recruited at the Cirrhosis Center Mainz of the University Medical Center of the Johannes Gutenberg-University in Mainz ($n = 157$) and the Department of Gastroenterology, Hepatology, Infectiology and Endocrinology of the Hannover Medical School ($n = 97$), both Germany, between 2019 and 2024. Of these 254 patients, 12 had PHES results available, but were unable or unwilling to perform the Stroop EncephalApp. These patients were excluded from further analyses, resulting in a cohort of 242 patients. All patients were either recruited in the outpatient departments or during hospitalization. Subgroups of this cohort have been previously used for other studies.^{7,13,14} The leading etiology of the underlying liver disease was determined according to clinical, serological, and histological findings. Diagnosis of cirrhosis was established by histology or a combination of conclusive appearance on ultrasound, radiological imaging, endoscopic features of portal hypertension, and medical history. Blood biochemistry was assessed in all patients. Patients were not approached for this study, or were excluded from the analyses, if they fulfilled one or more of the following criteria: HE \geq grade 1 according to the West Haven criteria, presence of a transjugular intrahepatic portosystemic shunt (TIPS), anamnestic ongoing alcohol consumption, presence of preterminal comorbidities, presence of hepatocellular carcinoma (HCC) outside of the Milan criteria, neurological comorbidities (i.e. dementia or history of stroke), or a history of recent head trauma.

For validation purposes, another cohort recruited at the Department of Internal Medicine I of the University Medical Center Halle (Germany) ($n = 104$) was included in the study. For this cohort, the same definitions and exclusion criteria were applied.

Diagnosis of HE

First, every patient was examined by an experienced hepatologist to rule out OHE or HE grade 1.

Testing for MHE was done using the portosystemic encephalopathy (PSE) syndrome test, which yields the PHES. Interpretation of PHES was done as previously described with norms for patients in Germany.¹⁵ Testing was never performed on the same day of any other intervention to exclude potential confounding factors. All tests were performed in a quiet, lit room between 09:00 h and 16:00 h. A score < -4 was considered pathological (termed 'PHES-MHE' throughout this report).¹⁵

Stroop EncephalApp was performed as described by Bajaj *et al.* and elsewhere.^{13,14,16} The test includes two states, an easier 'off' state and a more difficult 'on' state. In the off state, patients select the appropriate color of presented signs. As an example, a nonverbal cue (e.g. ###) is presented in the color red. The patient has to respond and press the button 'red'. In the more difficult on state, discordant-colored stimuli are presented. Here, the ink color and the word refer to different colors. Examples of the on and off state are displayed in Fig.

S1. During the test runs, the states are quizzed by a pre-defined algorithm before the app progresses to the next task: two practice off runs followed by five correct test off runs followed by the same routine for on runs. Each run stops when an error occurs and the patient has to repeat the run. Currently, for the complete Stroop EncephalApp, only raw cut-offs without adjustment for age or education are available for Germany.¹³

In addition, a subset of the cohort was tested with the ANT. For the ANT, patients were asked to name as many animals as possible in 1 min. Repeats and errors were excluded from the calculations. The number of named animals after 1 min was defined as the score. To compensate for the influence of age and education on the results in ANT, we calculated the simplified ANT (S-ANT1), which has been proposed by Campagna *et al.*⁶ A score of <20 animals was considered pathological.¹⁷

Ethics

The study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki and its later amendments. The study was approved by the ethics committee of the Landesärztekammer Rheinland-Pfalz (Nr. 2019-14483), of the MLU Halle-Wittenberg (Nr. 2018-75) and of the Hannover Medical School (No. 9826_BO_s_2021). Written informed consent was obtained from all participants.

Statistical analysis

Data were analyzed using IBM SPSS Statistic Version 29.0 (IBM Corporation, Armonk, NY, USA) and GraphPad Prism Version 8.0.2 (GraphPad Software, La Jolla, CA, USA). Quantitative data are expressed as medians with IQR and pairwise comparisons for quantitative variables were performed with an unpaired *t* test or with the Mann-Whitney U test, as appropriate. Categorical variables are expressed as frequencies with percentages. A chi-square test was applied for the comparison of two patient groups.

To assess a nonlinear association of age and performance in off runs in patients without PHES-MHE, age was fitted using a restricted cubic spline with four knots. We used the cohort of patients without PHES-MHE for this analysis to avoid confounding by MHE.

To investigate how runs of the EncephalApp Stroop or ANT discriminate between patients with and without PHES-MHE, we calculated the area under the receiver operating characteristic curve (AUROC) and its respective 95% CI. Comparisons between AUROC curves were performed using the method of Hanley.¹⁸

QuickStroop was built based on a linear regression model with predefined variables (age, school education, and time needed for the first two runs in the off state). Thresholds for QuickStroop were determined based on the Youden's Index. Additionally, cut-offs with a sensitivity of at least 90% were also determined. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated.

For all tests, we used $p < 0.05$ to define statistically relevant deviations from the respective null hypotheses. Given that our complete data analysis is exploratory, *p* values have to be interpreted in the context of the design and no adjustments for multiple testing were performed.

Table 1. Demographics and clinical characteristics of the study cohorts, at the time of study inclusion.

Variable	Development cohort (n = 242)	Validation cohort (n = 104)	p value
Center(s)	Mainz, Hannover	Halle	—
Age, year (IQR)	58 (51–65)	63 (54–69)	0.002
Female gender, n (%)	73 (30.2)	32 (30.8)	0.911
School education, year (IQR)	10 (9–11)	10 (8–10)	0.003
Etiology			
Alcohol, n (%)	112 (46.3)	66 (63.5)	<0.001
MASLD, n (%)	41 (16.9)	10 (9.6)*	
MetALD, n (%)	17 (7.0)	—	
Viral hepatitis, n (%)	25 (10.3)	2 (1.9)	
Cholestatic/autoimmune, n (%)	25 (10.3)	12 (11.5)	
Other, n (%)	22 (9.1)	14 (13.5)	
Median MELD score (IQR)	12 (9–16)	11 (9–15)	0.678
Child-Pugh A/B/C, n (%)	98/118/26 (40.5/48.8/10.7)	20/64/20 (19.2/61.5/19.2)	<0.001
History of ascites, n (%)	130 (53.7)	82 (78.8)	<0.001
Sodium, mmol/L (IQR)	138 (136–140)	138 (136–141)	0.059
Albumin, g/L (IQR)	33 (28–39)	34 (29–39)	0.586
Creatinine, mg/dl (IQR)	0.9 (0.7–1.2)	0.9 (0.8–1.3)	0.629
Platelets, /nl (IQR)	106 (71–165)	122 (87–213)	0.022
PHES (IQR)	-2 (-5–0)	-3 (-7; -1)	0.085
PHES-MHE, n (%)	76 (31.4)	38 (36.5)	0.352
Off + on time, sec (IQR)	182.6 (161.0–217.1)	203.4 (175.2–249.9)	<0.001
Off runs 1 + 2, sec (IQR)	34.5 (29.8–40.2)	38.1 (32.9–46.0)	<0.001
Off runs 1 - 3, sec (IQR)	51.1 (44.7–59.8)	56.4 (49.6–67.6)	<0.001
Off runs 1 - 4, sec (IQR)	68.3 (59.2–79.7)	75.0 (66.3–90.2)	<0.001
S-ANT1, n (IQR)	21 (17; 26) [†]	23 (18–28)	0.011

*Given that the cohort of patients from Halle was collected strictly before the new definition of MASLD, all patients with an alcohol consumption >20–30 g/day were considered to have alcohol-related liver disease and, thus, no separation between alcoholic liver disease and MetALD was performed.

[†]Available in 163 patients. Data are expressed as medians and IQRs or as frequencies and percentages; MASLD, metabolic dysfunction-associated steatotic liver disease; MetALD, MASLD and increased alcohol intake; MELD, model for end-stage liver disease; MHE, minimal hepatic encephalopathy; PHES, Psychometric Hepatic Encephalopathy Score; S-ANT1, simplified Animal Naming Test.

Results

Demographics and baseline characteristics of the cohort

The development cohort comprised 242 patients, whereas the validation cohort included 104 patients. Characteristics and a comparison between the derivation and validation cohorts are displayed in Table 1. The cohorts mainly differed in terms of age and liver function.

Diagnostic accuracy of different off and on runs to diagnose PHES-MHE

First, we compared the discriminative ability of various off and on run combinations, including the total off + on time for detection of PHES-MHE. There was no significant difference between the AUROC for the first two off runs compared with the total time ($p = 0.53$) (Table 2). Correspondingly, none of the other run combinations differed regarding their discriminative ability when compared with the total time.

Development of the QuickStroop regression formula

Given that age heavily affects performance in the Stroop test and that the relationship between the two is mostly nonlinear, we first looked at the correlation between age and performance in off runs 1 + 2 in patients without PHES-MHE using a

restricted cubic spline (Fig. 1). Here, we noted an increase in the influence of age on time needed for off runs 1 + 2 in patients over 60 years of age. Consequently, we decided to build different regression formulae for patients ≥ 60 and < 60 years of age. The regression model (termed 'QuickStroop') was built as described in the Statistics analysis section and was as follows:

PHES-MHE in patients ≥ 60 years of age = $0.5012 - (0.053 \times \text{age}) - (0.184 \times \text{school years}) + (0.109 \times \text{off runs 1 + 2})$.

PHES-MHE in patients < 60 years of age = $-13.8183 - (0.099 \times \text{age}) + (0.445 \times \text{school years}) + (0.408 \times \text{off runs 1 + 2})$.

A score ≥ 0 predicted PHES-MHE (according to Youden's index). We did not include gender in the regression models, because neither total time ($p = 0.271$) nor time needed for off runs 1 + 2 ($p = 0.331$) differed between women and men in the group of patients without PHES-MHE.

We also built the regression formula for total time (off + on):

PHES-MHE in patients ≥ 60 years of age = $0.8069 - (0.093 \times \text{age}) - (0.12 \times \text{school education}) + (0.032 \times \text{total time})$ (AUROC: 0.93).

PHES-MHE in patients < 60 years of age = $-11.2177 - (0.1 \times \text{age}) + (0.228 \times \text{school years}) + (0.078 \times \text{total time})$ (AUROC: 0.85).

A score ≥ 0 predicted MHE.

The median time needed to conduct QuickStroop was 34.5 s (IQR 29.8–40.2 s) in the development cohort and 38.1 s (IQR

Table 2. AUROCs for various off run combinations compared with the total time.

	Total time (on + off)	Off runs 1 + 2	Off runs 1 - 3	Off runs 1 - 4
AUROC (95% CI)	0.86 (0.81–0.90)	0.83 (0.78–0.88)	0.84 (0.79–0.89)	0.84 (0.79–0.89)
p value vs. total time	—	0.53	0.64	0.76

AUROC, area under the receiver operating characteristic curve.

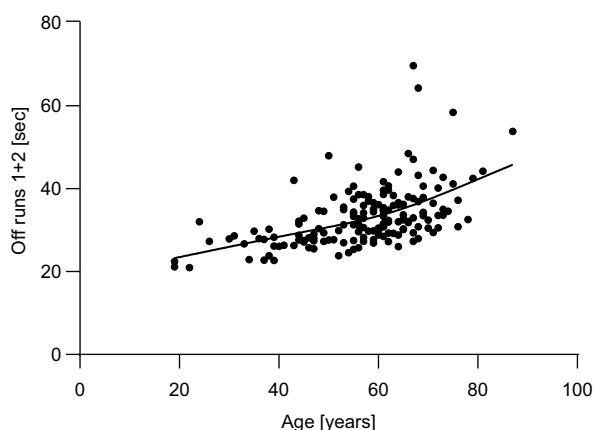


Fig. 1. Non-linear association of age and performance in off runs in patients without PHES-MHE. A restricted cubic spline with four knots was fitted. MHE, minimal hepatic encephalopathy; PHES, psychometric hepatic encephalopathy score.

32.9–46.0 s) in the validation cohort, whereas the time needed to conduct the complete Stroop EncephalApp was 182.6 s (IQR 161.1–217.1 s) and 203.4 s (IQR 175.2–249.9 s), respectively.

Diagnostic accuracy of QuickStroop in the development and validation cohorts

QuickStroop discriminated between patients with and without PHES-MHE with an AUROC of 0.88 in the development cohort

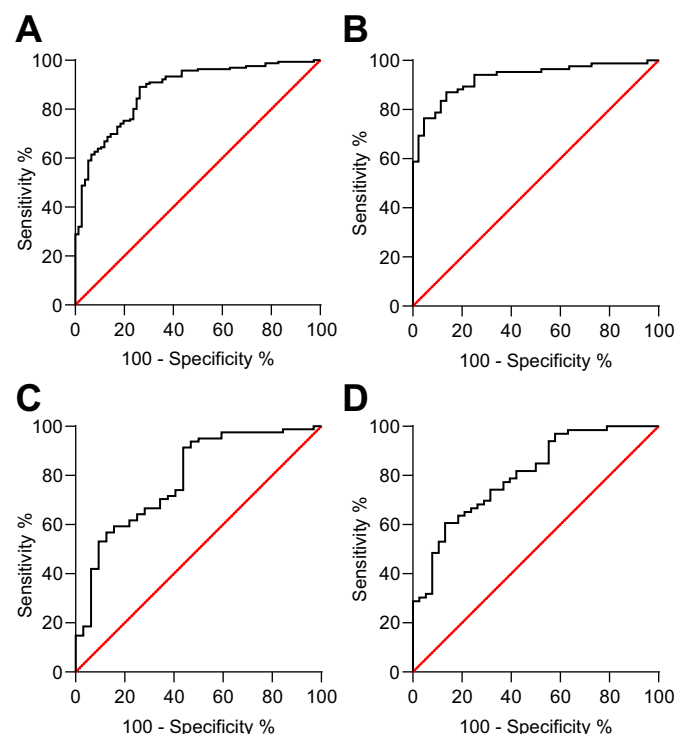


Fig. 2. AUROC curve of QuickStroop for prediction of PHES-MHE in different subgroups. (A) AUROC curve of QuickStroop in: (A) complete development cohort (AUROC: 0.88), (B) patients <60 years of age (AUROC: 0.93), (C) patients ≥60 years of age (AUROC: 0.79), and (D) in the validation cohort (AUROC: 0.81). AUROC, area under the receiver operating characteristic curve; MHE, minimal hepatic encephalopathy; PHES, psychometric hepatic encephalopathy score.

and an accuracy of 84% (sensitivity: 74%, specificity: 89%) (Fig. 2A, Table 3). In patients ≥60 years of age, the AUROC was 0.79, while it was 0.93 in patients <60 years of age (Fig. 2B/C, Table 3). In the validation cohort, the acceptable discriminative ability of QuickStroop was maintained with an AUROC of 0.81 and an accuracy of 73% (sensitivity: 62%, specificity: 79%) (Fig. 2D, Table 3). In patients ≥60 years of age, AUROC was 0.81, while it was 0.82 in patients <60 years of age. Sensitivity, specificity, PPV, and NPV of QuickStroop for the prediction of PHES-MHE in both cohorts are displayed in Table 3.

We also identified cut-offs in both age groups with a sensitivity of at least 90% to provide the opportunity to use QuickStroop as a prescreening test before potential elaborate testing with PHES. The respective cut-offs were −0.4771 and −1.1897 for the age groups <60 years and ≥60 years, respectively. The sensitivity, specificity, PPV, and NPV using these cut-offs in the development and the validation cohort are displayed in Table 3. Of note, further testing with PHES would have been avoided in 48% and 36% of the patients of the development and validation cohort, respectively, if QuickStroop had been used as a prescreening tool.

Comparison of QuickStroop with the ANT for detection of PHES-MHE

Results in S-ANT1 were available in a subcohort of 163 patients (34% with PHES-MHE) in the development cohort. In this cohort, QuickStroop (AUROC 0.86) had a better ability to discriminate between patients with and without PHES-MHE compared with S-ANT 1 (AUROC 0.70) ($p = 0.005$). There was no difference between QuickStroop (AUROC 0.74) and S-ANT1 (0.75) in the subcohort of patients ≥60 years ($p = 0.91$), whereas QuickStroop (AUROC 0.92) was superior compared with S-ANT1 (AUC 0.66) in patients <60 years ($p < 0.001$). In the validation cohort, results in S-ANT1 were available for all 104 patients. QuickStroop had a numerically better discriminative ability compared with S-ANT1; however, this did not reach significance (AUROC 0.81 vs. 0.73, $p = 0.26$). Results for sensitivity, specificity, PPV, and NPV for both QuickStroop and S-ANT1 in the development and validation cohorts are displayed in Table S1.

Discussion

Detection of MHE is important because it negatively affects patient well-being and is treatable. In this study, we validated QuickStroop, a shortened version of the Stroop EncephalApp, for patients in Germany with liver cirrhosis, and demonstrated an acceptable discriminative ability to identify patients with PHES-MHE. Additionally, we found that, especially in younger patients, QuickStroop appeared superior to ANT for identifying patients with PHES-MHE.

Testing for MHE is frequently neglected in routine clinical practice, mostly due to time restrictions.^{8,9} To overcome this issue, Acharya *et al.*¹¹ introduced QuickStroop for rapid screening for low grades of HE in patients from the USA.^{11,19} The finding that a shortened version of the Stroop EncephalApp might be applicable to identify patients with MHE has also been demonstrated in Japan by Hanai and colleagues.²⁰ Here, the authors found that two runs of the on state were best for separating patients with and without covert hepatic encephalopathy

Table 3. Discriminative ability of QuickStroop for detection of PHES-MHE.

QuickStroop	AUROC (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Accuracy, %
Development cohort	0.88 (0.84–0.92)	74 (62–83)	89 (83–93)	65 (64–85)	88 (82–92)	84
Patients <60 years of age	0.93 (0.89–0.97)	86 (72–94)	87 (78–93)	78 (63–88)	93 (84–97)	87
Patients ≥60 years of age	0.79 (0.69–0.88)	72 (50–87)	84 (74–91)	56 (38–73)	91 (82–96)	81
Validation cohort	0.81 (0.72–0.89)	62 (45–76)	79 (66–87)	63 (46–78)	77 (65–86)	73
With 'sensitivity cut-offs' (development cohort)*	—	91 (81–96)	66 (58–73)	55 (46–64)	94 (88–97)	—
With 'sensitivity cut-offs' (validation cohort)*	—	87 (71–95)	49 (36–61)	49 (40–62)	87 (70–95)	—

*Sensitivity cut-offs: age <60 years, <0.4771; age ≥60 years, −1.1897; AUROC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value.

according to PHES. In our current study, we validated the findings by Acharya *et al.*¹¹ for patients in Germany with cirrhosis and also found that the first two runs of the off state have a comparable discriminative ability as the total time in the Stroop EncephalApp. However, there are also relevant differences between the study by Acharya *et al.*¹¹ and ours that have to be considered when interpreting the findings. We did not add gender into the regression models for QuickStroop, because we did not find any differences in times needed for off runs between women and men in the group of patients without PHES-MHE. In contrast to Acharya *et al.*¹¹ and Hanai *et al.*,²⁰ we also excluded patients with a history of OHE, because testing for MHE in patients with a history of OHE is not meaningful for treatment decisions.^{11,20} Additionally, in the United States-based study, no patients above the age of 65 years were recruited, limiting the implementability of QuickStroop in routine care. In our current study, we did not set a predefined age limit. In this context, we noticed that the influence of age on performance in the Stroop test increased from the age of 60 years. Therefore, we built separate regression models for older (≥60 years) and younger (<60 years) patients. When analyzing these cohorts separately, we also noted that the discriminative ability of QuickStroop to identify patients at risk for PHES-MHE was only mediocre in the older group, whereas it is better in the younger group. Of note, the sensitivity of QuickStroop to identify patients at risk for PHES-MHE in the older group was especially poor. For everyday clinical practice, this means that QuickStroop should be used with more caution in older patients, whereas it appears to be an applicable tool for younger patients. This might be explained by the fact that there could be a larger group in the subgroup of patients aged ≥60 years who are less familiar with the use of tablets or smartphones. Being less familiar with tablets or smartphones might influence performance in the Stroop EncephalApp. In addition, the risk for cerebrovascular injury leading to neurocognitive disorders besides HE is higher in older patients. In our contemporary cohort, the main etiologies of cirrhosis were alcohol or metabolic disease, which are associated with cerebral injury. Therefore, it has to be emphasized that the Stroop test is not specific to detect MHE and results might be influenced by confounding factors. This was recently highlighted by a study by Sultanik *et al.* demonstrating that about one-third of outpatients with neurocognitive complaints did not have MHE and 75% of the patients with MHE had at least one other cause for a neurocognitive disorder.²¹ Although this cohort is not completely comparable with our current cohort, it might be possible that, in some cases, pathological results in QuickStroop might have been caused by disorders other than MHE in our cohort.

The ANT has emerged as one of the most frequently used screening tests for MHE in routine clinical practice and has been validated in several countries throughout the past few years.^{12,17,22–24} Until now, there has only been one comparison between ANT and a shortened version of the Stroop EncephalApp.²⁵ In their study, Ortiz Trevino *et al.* found comparable AUROCs between two runs in the off state and ANT (0.75 vs. 0.73). However, the authors only analyzed raw off runs without implementing age and education as variables. Our data demonstrated that QuickStroop appears to be superior to ANT for identifying patients at risk for PHES-MHE at least in the subgroup of patients aged <60 years. However, in patients ≥60 years of age, the performances of QuickStroop and ANT were comparable in the development cohort. When analyzing the discriminative ability of QuickStroop and ANT for detection of patients at risk for PHES-MHE in the older patient subgroup, it has to be acknowledged that AUROCs of both tests were only mediocre, questioning the usability for therapeutic decisions in clinical practice. In addition, we found a poor performance of ANT in patients <60 years of age, indicating that therapeutic decisions should not be made based solely on results in ANT in this group.

QuickStroop appears to be a valuable tool for implementing an initial screening for MHE in routine care outside of specialized clinics focusing on HE research.²⁶ However, this mostly applies to patients <60 years of age, whereas, in older patients, QuickStroop should be interpreted with more caution. In this context, it has to be emphasized that PHES will remain the gold standard for detection of MHE in patients with cirrhosis. This was also reiterated by a recently published paper comparing available HE tests.¹⁴ Here, the authors emphasized the need for adequate norm values, which are only rigorously available in most cases for PHES. Our study provides the basis for an algorithm in which QuickStroop can be used as a prescreening tool, for example by applying the sensitivity cut-offs, and subsequently confirming or excluding the diagnosis of MHE using PHES. Now, future studies have to prove that QuickStroop is sensitive to therapeutic trials with lactulose or even nutrition, which might lead to a resolution of PHES-MHE, and is also robust regarding learning effects.^{27,28} Notably, this important point has recently been proven for ANT.²⁹

In conclusion, we provide regression formulae for QuickStroop for identifying patients with PHES-MHE. Although the definitive diagnosis of MHE should be made based on a validated test, such as PHES, QuickStroop appears to be useful for clinical practice as a screening test, especially in younger ones.

Affiliations

1. Department of Internal Medicine I, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany; 2. Cirrhosis Center Mainz, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany; 3. Department of Gastroenterology, Hepatology, Infectious Diseases and Endocrinology, Hannover Medical School, Hannover, Germany; 4. Department of Neurology, Hannover Medical School, Hannover, Germany; 5. First Department of Internal Medicine, Martin-Luther University Halle-Wittenberg, Halle, Germany; 6. Internal Medicine IV, Jena University Hospital, Jena, Germany

Abbreviations

ANT, Animal Naming Test; AUROC, area under the receiver operating characteristic curve; HCC, hepatocellular carcinoma; HE, hepatic encephalopathy; MASLD, metabolic dysfunction-associated steatotic liver disease; MELD, Model of end-stage liver disease; MetALD, MASLD and increased alcohol intake; MHE, minimal hepatic encephalopathy; NPV, negative predictive value; OHE, overt hepatic encephalopathy; PHES, Psychometric Hepatic Encephalopathy Score; PPV, positive predictive value; PSE, portosystemic encephalopathy; S-ANT1, simplified animal naming test; TIPS, transjugular intrahepatic portosystemic shunt.

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Conflicts of interest

AMS reports receiving travel expenses from Abbvie and Boehringer Ingelheim. SJG reports receiving travel and accommodation expenses from Ipsen and Gilead. CL reports consulting honoraria from Norgine, Merz Therapeutics, Ipsen, and Boehringer Ingelheim, lecture fees from Norgine, Intercept Pharmaceuticals/ Advanz Pharma, Gilead Sciences, Boehringer Ingelheim, Falk Foundation, and Merz Therapeutics, and research grants from Norgine and Merz Therapeutics. CR reports consulting honoraria from Boehringer Ingelheim, and lecture fees from Bristol-Myers, Gore and Falk Foundation. The other authors have no potential financial or nonfinancial conflict of interests regarding this study. All mentioned conflicts of interest are unrelated to this research.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Performed research: CL, SJG, LK, AFE, EMS, SM, JFME, MMG, PRG, HW, AZ, CR, RG, BM. Contributed to acquisition of data: CL, SJG, LK, AFE, EMS, SM, JFME, MMG, PRG, HW, AZ, CR, RG, BM. Designed the experiments and analyzed the data: CL, KW, AZ, CR, RG, BM. Contributed reagents/materials/analysis tools: CL, PRG, KW, CR, RG, BM. Wrote the paper: CL. Critical revision of the paper: all authors.

Statistical analysis: CL. All authors approved the final version of the manuscript and the authorship list. Guarantor of the article: CL.

Data availability statement

Raw data are available from the corresponding author on reasonable request.

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Supplementary data

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Author names in bold designate shared co-first authorship

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