# PRELIMINARY REPORT OF THE HEPATIC ENCEPHALOPATHY ASSESSMENT DRIVING SIMULATOR (HEADS) SCORE

**Introduction:** Audiovisual simulations of reallife driving (ie, driving simulators) have been used to assess neurologic dysfunction in a variety of medical applications. However, the use of simulated driving to assess neurologic impairment in the setting of liver disease (ie, hepatic encephalopathy) is limited.

**Objectives:** The aim of this analysis was to develop a scoring system based on simulated driving performance to assess mild cognitive impairment in cirrhotic patients with hepatic encephalopathy.

**Methods:** This preliminary analysis was conducted as part of the Hepatic Encephalopathy Assessment Driving Simulator (HEADS) pilot study. Cirrhotic volunteers initially underwent a battery of neuropsychological tests to identify those cirrhotic patients with mild cognitive impairment. Performance during an audiovisually simulated course of on-road driving was then compared between mildly impaired cirrhotic patients and healthy volunteers. A scoring system was developed to quantify the likelihood of cognitive impairment on the basis of data from the simulated on-road driving.

**Results:** Mildly impaired cirrhotic patients performed below the level of healthy volunteers on the driving simulator. Univariate logistic regression and correlation models indicated that several driving simulator variables were significant predictors of cognitive impairment. Five variables (run time, total map performance, number of collisions, visual divided attention response, and average lane position) were incorporated into a quantitative model, the HEADS scoring system. The HEADS score (0–9 points) showed a strong correlation with cognitive impairment as measured by area under the receiver-operator curve (.89).

**Conclusion:** The HEADS system appears to be a promising new tool for the assessment of mild hepatic encephalopathy. (*Ethn Dis.* 2008;18:357–364)

**Key Words:** Cirrhosis, Neuropsychological Tests, Scoring System

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### INTRODUCTION

Cognitive impairment in the setting of liver disease is referred to as hepatic encephalopathy (HE), a multifactorial disorder that results in part from impaired detoxification by a diseased liver. Even mild HE (clinical symptoms not obvious) can have substantial consequences to the patient, including impaired activities of daily living and a reduction in overall quality of life.<sup>1</sup> Mild HE is a neurocognitive complication of cirrhosis that is associated with poor quality of life, increased rate of progression to overt HE, and driving skill impairment.<sup>2–4</sup>

Diagnostic criteria for mild HE includes abnormal brain electrophysiology by electroencephalogram or impaired neuropsychological testing in the absence of gross changes on mental status or neurologic examination.<sup>5</sup> In a recent study involving anonymous questionnaires sent to members of the Association for the Study of Liver Disease, most members believed that mild HE was a major problem and that routine testing of cirrhotic patients for mild HE should be considered. However, routine neuropsychological testing has limitations: clinic visit time is increased (time may exceed three hours), the testing is difficult, specialized personnel are needed, and the tests are not standardized.<sup>2</sup> Therefore, we hypothesized that the assessment of mild HE could be improved by developing a short (10-30 minutes), practi-

Address correspondence and reprint requests to: Scott L. Nyberg, MD, PhD; Mayo Clinic College of Medicine; 200 First St SW; Rochester MN, 55905; 507-266-6772; 507-266-1856; nyberg.scott@ mayo.edu cal, and quantifiable task such as a computer-based driving simulator routine. The use of a driving simulator to assess driving performance of patients with chronic liver disease has been limited to a preliminary report.<sup>6</sup> Investigators compared driving parameters between groups of impaired and unimpaired cirrhotic patients; however, development of a scoring system to quantify impairment was not considered in their preliminary report.

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The goal of the current analysis was twofold: 1) develop a driving simulator routine capable of assessing mild HE, the HEADS (<u>Hepatic Encephalopthy</u> <u>Assessment Driving Simulator</u>) system and 2) develop a preliminary model based on HEADS data for the quantitative assessment of mild HE.

# **METHODS**

#### Study Sample

Approval was obtained from the Mayo Clinic Institutional Review Board and the executive committee of our outpatient General Clinical Research Center (GCRC) to conduct a pilot

study. All subjects were considered eligible if they were 18-70 years of age, were not pregnant, spoke English as their primary language, possessed a driver's license, and provided written informed consent. Healthy subjects were eligible if they had no major medical problems, including no history of liver disease. Cirrhotic subjects were eligible if they had been approved and were awaiting liver transplantation. Exclusion criteria for all participants included a history of severe motion sickness, history of a major psychiatric disorder, or gross evidence of HE (grade I or greater by Westhaven criteria) at the time of testing.<sup>7</sup>

## Study Overview

This study consisted of two sequential pilot studies involving healthy and cirrhotic participants. Healthy participants were studied first and underwent driving simulator testing to assess its feasibility and to determine standard values in a normal population. Cirrhotic participants were tested later with the same driving simulator hardware and software. No attempt was made to match the cirrhotic patients and healthy volunteers in this pilot study. In addition to the driving simulator testing, the cirrhotic patients underwent a battery of neuropsychological tests to assess their level of cognitive impairment. Cirrhotic participants underwent neuropsychological testing as part of their pretransplant workup. Driving performance of cognitively impaired cirrhotic patients and that of healthy volunteers were compared. Correlations were made between the neuropsychological data and driving simulator data obtained from the impaired cirrhotic participants. All study participants completed questionnaires regarding their age, level of education, history of motion sickness before testing, and presence of simulator sickness (dizziness, nausea, or headache) after simulated driving.

Neuropsychological Test **Cognitive Domain** California Verbal Learning Test Long Delay Free Recall Memory Trails Test 1-5 Learning Grooved Pegboard Test Dominant Hand Motor Nondominant Hand Motor Wechsler Memory Scale - Third Edition Age-Adjusted Score Logical Memory 1 Learning Logical Memory 2 Memory Verbal Paired Associates 1 Learning Verbal Paired Associates 2 Memory Perceptual Organization Index Visual Acuity Processing Speed Index Concentration Rey-Osterrieth Complex Figure Test Visual Acuity Trailmaking B Score Concentration Working Memory Index Attention

#### Table 1. Cognitive domains assessed by neuropsychological tests during pilottesting of the Hepatic Encephalopathy Assessment Driving Simulator (HEADS) system

# Neuropsychological Testing

Cirrhotic study participants underwent a battery of neuropsychological tests to establish the presence and extent of impairment in six specific cognitive domains of motor, attention, memory, visual acuity, learning, and concentration. The specific tests used to assess each domain are summarized in Table 1. Zscores were determined by using standard techniques and normative data for all neuropsychological data collected. All cognitive domain scores were determined by the average of Z-scores from corresponding tests outlined in Table 1. Impairment in each domain was defined by an average Z-score for that domain of -1 or lower. Cirrhotic patients with an impairment in at least one cognitive domain were defined as having mild HE for the purpose of this study.

### **Driving Simulator**

All study participants were tested on the same driving simulator, Systems Technology, Inc. (STI) Simulator Model 300 driving simulator with digital control interface and active steering (STI, Hawthorne, Calif) (Figure 1). The driving simulator hardware and software were based on a desktop computer station with a variety of offthe-shelf components. The test subjects interact with a driving simulator that uses a single monitor, active steering wheel, foot accelerator, brake pedals, speedometer, and tachometer. Two working programs were developed: one of a 2.5-mile course (Acclimation Run,  $\approx 2-5$  minutes) and the second of a 10-mile course (Formal Run, ≈15-30 minutes). The 10-mile Formal Run included a drive through both urban and rural areas and a brief car-following routine. Multiple visual tasks were presented to the drivers to assess their ability to divide attention while driving during the Formal Run. Road maps were also provided on the screen to test the driver's ability to follow visual instructions and to assess short- and longterm memory. Raw data of 43 simulated driving variables were collected during the 10-mile Formal Run as summarized in Table 2. In addition, total map performance (sum of score of all three maps) and total collisions (sum of all collisions) were determined from raw data. We refer to the combination of hardware and software as the HEADS system.

### **HEADS Score**

Univariate logistic regression and correlation models indicated that several

driving simulator variables were significant predictors of general cognitive impairment. An intuitive approach based on these statistical data was used to create the preliminary HEADS scoring system. This model was based on five variables collected during the simulated drive: total map performance, run time, average lane position, total collisions, and visual divided attention response. The coefficients for the model were determined by using logistic regression and data from both healthy volunteers and cirrhotic patients.

# RESULTS

Healthy participants (n=31) were enrolled to provide standard values for the driving simulator. This cohort consisted of healthy employees, friends, and family members. Of this group, 38.7% were men, all had a college degree or greater level of education, and their mean age was 39 years (Table 3). The average time to complete driving simulator testing for the healthy cohort was 1280.5±175.2 seconds (21.33 minutes) (Table 4). Overall this group performed as expected. For example, 66.7% were not involved in pedestrian collisions and 69.7% performed the most difficult map sequence (Map3) correctly. From questionnaire data, 9.7% (3/31) of participants who completed the run experienced nausea for at least two hours. Nausea did not occur at any specified or reproducible time but randomly during or after testing. No participants experienced headache, vomiting, or inability to complete the run, which indicates that healthy participants performed without moderate adverse events.

Fifteen cirrhotic patients underwent both neuropsychological testing and simulated driving with the HEADS system. Two other cirrhotic patients attempted the HEADS testing but withdrew because of nausea. Thirteen of 15 cirrhotic patients who completed testing were diagnosed with mild HE based on



Fig 1. STI Simulator Model 300 customized as HEADS system

impairment in at least one cognitive domain by neuropsychological testing; two cirrhotic patients were cognitively unimpaired. When cirrhotic patients were compared to healthy volunteers, a significant difference was observed in the distribution of sex, age, and level of education (Table 3).

Cognitive impairment had a negative effect on several parameters of driving performance (Table 4). The average time to complete driving simulator testing for the cognitively impaired cirrhotic cohort was 1533.9±313.4 seconds (25.5 minutes). There was a significant difference (P=.017) in time to completion between groups. Impaired cirrhotic patients were significantly more likely to hit a pedestrian (69.2% involved in one or two collisions) than were healthy controls (33.3% involved in one or two collisions) (P=.01). Compared with the percentage of healthy subjects (30.3%), a higher percentage of impaired (69.2%) (P=.02), visually impaired (83.3%) (P=0.03), and motor-impaired cirrhotic patients (62.5%) (nonsignificant) did not perform Map3. From questionnaire data, 20% (3/15) of cirrhotic participants who completed the run experienced at least two hours of nausea. No cirrhotic participants experienced headache or vomiting.

Univariate logistic regression showed a significant correlation between two driving simulator variables and cognitive impairment as determined by a Z-score less than -1 in any neuropsychological domain: run time (seconds), odds ratio (OR) 1.004 (P=.002); and total collisions (number), OR 4.84 (P=.007). Univariate correlation showed that three driving simulator variables correlate well with neuropsychological tests: total map performance,  $R^2 = .54$  (P = .002); visual divided attention response,  $R^2 = .33$ (P=.02); and average lane position,  $R^2$ =.31 (P=.03). These results suggest that data collected during the driving simulator routine correlated with the cognitive impairment of cirrhotic individuals detected by neuropsychological testing.

Five driving simulator variables that showed the strongest correlation with the various domains of cognitive im-

Table 2	List of simulated	driving variables	measured by	the HEADS system
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Variable	Units	Definition			
Assessment Driving Simulator (HEADS) system					
Avg Lane 1	feet	Average lane position - interval 1 (12750 to 15250 feet)			
Avg Lane 2	feet	Average lane position - interval 2 (29000 to 32200 feet)			
Lane Dev 1	feet	How well participant was able to stay in lane during interval 1			
Lane Dev 2	feet	How well participant was able to stay in lane during interval 2			
Off Road	#	Number of times the tires went off the right edge of the road			
Center Xing	#	Number of times the tires crossed the roadway center line			
Excess Ay	#	Number of times the driver exceeded a lateral acceleration of .25 g's			
Avg Speed 1	miles per hour	Average speed during interval 1			
Avg Speed 2	miles per hour	Average speed during interval 2			
Speed Dev 1	miles per hour	Speed deviation during interval 1			
Speed Dev 2	miles per hour	Speed deviation during interval 2			
Tailgates	#	Number of times the driver was within 30 feet of a lead vehicle			
Avg TailGate	feet	Average distance the driver was behind the vehicles during all tailgate occurrences			
Tailgate Dev	feet	Distance deviation the driver was behind the vehicles during all tailgate occurrences			
Time Over Speed	%	Percentage of the run time where the driver was over the speed limit			
Dist Over Speed	%	Percentage of the run distance where the driver was over the speed limit			
Excess Speed	#	Number of times the driver drove at an excessive speed (>1.3 * speed limit)			
Time @ Excess	%	Percentage of the run time where the driver was over the excessive speed threshold			
Dist @ Excess	%	Percentage of the run distance where the driver was over the excessive speed threshold			
Collisions	#	Total number of collisions with other vehicles			
Off Road Acc	#	Total number of accidents that occurred because the driver went too far off the road			
Ped Collisions	#	Total number of collisions with pedestrians			
Stop Sign Infr	#	Total number of stop sign infractions			
Signal Light Infr	#	Total number of signal light infractions			
Stops @ Red	#	Total number of times the driver stopped at a red light			
Map1 Performance	#	Specifies if the driver followed the first map route correctly (0) or incorrectly (1)			
Map2 Performance	#	Specifies if the driver followed the second map route correctly (0) or incorrectly (1)			
Map3 Performance	#	Specifies if the driver followed the third map route correctly (0) or incorrectly (1)			
Words Correct	#	Number of correct responses that occurred during the word recognition task			
Words Incorrect	#	Number of word recognition responses where the driver responded incorrectly			
Words Missed	#	Number of word recognition responses where the driver did not respond in the time allowed			
Avg Word Response	seconds	Average response time for the correct word recognition responses			
Word Response Dev	seconds	Response time deviation for the correct word recognition responses			
VDA Correct	#	Number of correct responses that occurred during the visual divided attention task			
VDA Incorrect	#	Number of visual divided attention tasks where the driver responded incorrectly			
VDA Missed	#	Number of visual divided attention tasks where the driver did not respond in the time allowed			
Avg VDA Response	seconds	Average response time for the correct visual divided attention task			
VDA Response Dev	seconds	Response time deviation for the correct visual divided attention task			
AQ Correct	#	Number of correct responses that occurred during the audio divided attention task			
AQ Incorrect	#	Number of audio divided attention tasks where the driver responded incorrectly			
AQ Missed	#	Number of audio divided attention tasks where the driver did not respond in the time allowed			
Avg AQ Response	seconds	Average response time for the correct audio divided attention task			
AQ Response Dev	seconds	Response time deviation for the audio visual divided attention task			

pairment were used to develop a quantitative model to determine the HEADS score. These five variables included 1) average lane position: a measure of lane position during the second half of the formal simulator run (correlated with memory and visual impairment); 2) total map performance: the number of maps that a participant failed to complete successively (correlated with attention and learning); 3) run time: a measurement of the total time in seconds to finish the formal run (correlated with motor impairment); 4) total collisions: the sum of all accidents including off road accidents, auto collisions, and pedestrian collisions (correlated with motor impairment); 5) visual divided attention (VDA) response: the average time for the participant to respond to VDA prompt on the screen (correlated with learning). The following multivariate model was developed by logistic regression with preliminary data from this pilot study:

HEADS score =

run time  $\times .0066 + average$  lane position

- $\times .252 + VDA$  response  $\times 1.59$
- map performance
- $\times .583 + total$  collisions  $\times .215 6.648$

The HEADS score ranged from 0 to 9, with 9 predictive of the poorest driving performance and greatest likeli-

	Healthy	Impaired Cirrhotic*	Non-impaired Cirrhotic
Total number studied (N)	31	13	2
Mean aget	38.7±10.29	$50.5 \pm 8.76$	54.0±9.90
% male	38.7	69.2	100
Level of Education‡	$17.6 \pm 2.09$	14.1±2.22	$15.5 \pm 3.54$
Mean MELD Score	N/A	$10.5 \pm 3.97$	$10.0 \pm 2.83$

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\* As defined by neuropsychological testing

† Age in years

\* Number of years of school attendance; 0-6: elementary; 7-12: junior and high school; 13-16: college; > 17: graduate school

N/A; not applicable

hood of neuropsychological impairment (Table 5). A score of 9 is the highest possible score. The HEADS score showed an excellent sensitivity and specificity with regards to predicting impairment by neuropsychological testing (Figure 2). Concordance, determined by area under the receiveroperator curve, of the HEADS score was .89 (.5= random chance, 1.0=perfect predictor). The estimated probability of impairment at each HEADS score is illustrated in Table 5. HEADS score and Model for End-stage Liver Disease (MELD) score were not significantly correlated in this small cohort of cirrhotic patients (Table 3).

# DISCUSSION

The principal finding of this study relates to the utility of a driving simulator to assess cognitive impairment in patients with mild HE determined by neuropsychological tests. These results demonstrate 1) that the HEADS system provided information on driving variables that correlated well with neuropsychological impairment and 2) that simulated driving information was combined to formulate a score with a relatively high predictive ability for the level of cognitive impairment of cirrhotic individuals. We expect that the current (preliminary) HEADS scoring system will undergo modification as new data are obtained from larger cohorts of patients representing a greater diversity of MELD scores.

The prevalence of mild HE in patients with cirrhosis is estimated to vary from 30% to 84%. This range results in part from differences in definitions and diagnostic modalities used in various studies.<sup>8</sup> This range also results in part from observed barriers to routine testing. Seventy-two percent of US-based American Association for the Study of Liver Disease (AASLD) members admit to testing less than half of their patient population for mild HE because it adds too much clinic time to a visit, requires specialized personnel to administer, and is expensive.<sup>2</sup> No gold standard for mild HE testing exists, and consequently the application of diagnostic tests is not uniform,<sup>9</sup> which may leave physicians with information that they can not interpret. Thus, a simple, rapid, quantifiable scoring system, such as HEADS, for diagnosis of mild HE would likely increase the probability of testing for mild HE in the future. In the current study, we used a battery of neuropsychological tests to assess cirrhotic participants on the transplant list. The high rate of our patients diagnosed with mild HE (13 of 15 cirrhotics) was likely a selection bias since only patients wait-listed for liver transplantation were eligible for this pilot study. Further studies are warranted to determine if the HEADS scoring system correlates well with all cirrhotic patients and other diagnostic tools used to assess populations of cirrhotic patients.

A validated scoring system that provides a quantitative basis for the description of HE from normal to clearly abnormal has not previously existed. Such a quantitative approach to assessing HE in the clinical setting would be preferred over the current pass/fail criterion. Thus, the HEADS scoring system may be useful clinically for such purposes as assessing response to therapy for HE.<sup>2,7,10</sup> Another potential application of the HEADS system is in assessing cognitive improvement after use of an extracorporeal liver support device, such as albumin dialysis<sup>6</sup> or a bioartificial liver.<sup>11,12</sup>

Numerous reports have shown a direct correlation between fitness to drive and level of encephalopathy during on-road evaluation.<sup>13</sup> A recent study of 274 consecutive patients with liver cirrhosis used on-road drive testing and identified a significant difference in driving ability of those with subclinical HE vs cirrhotic patients without subclinical HE (P < .05).<sup>3</sup> Driving ability was based on three global driving categories: car handling, adaptation to traffic situation, and cautiousness in maneuvering. These variables are similar to what we deemed significant predictors of cognitive impairment in our study: run time, number of collisions, and average lane position. The problem with using on-road driving to test for cognitive impairment is that it may be hazardous. However, the on-road driving test remains the gold standard. A computer-based alternative, such as a driving simulator, would address the paucity of data comparing driving performance of patients with mild HE to that of matched healthy controls. Whether the HEADS scoring system

#### Table 4. HEADS driving variables: healthy subjects vs. impaired cirrhotics

HEADS variable		Healthy <i>N</i> =31	Impaired Cirrhotic N=13	P value
Run time (seconds)	Mean (SD)	1280.5 (175.2)	1533.9 (313.4)	.017
Avg Lane 1 (feet)	Mean (SD)	7.1 (3.8)	8.5 (4.6)	.979
Avg Lane 2 (feet)	Mean (SD)	9.0 (4.1)	10.9 (4.3)	.123
Lane Dev 1 (feet)	Mean (SD)	0.9 (0.3)	1.5 (1.47)	.374
Lane Dev 2 (feet)	Mean (SD)	1.6 (1.0)	2.0 (1.1)	.288
Off Road (#)	Mean (SD)	1.7 (1.5)	1.5 (1.1)	.447
Center Xing (#)	Mean (SD)	6.3 (2.9)	8.5 (5.0)	.337
Excess Ay (#)	Mean (SD)	7.1 (4.3)	6.4 (4.7)	.842
Avg Speed 1 (miles per hour)	Mean (SD)	50.0 (6.0)	46.7 (11.8)	.593
Avg Speed 2 (miles per hour)	Mean (SD)	51.3 (7.4)	45.8 (9.2)	.067
Speed Dev 1 (miles per hour)	Mean (SD)	3.0 (0.7)	3.4 (1.4)	.803
Speed Dev 2 (miles per hour)	Mean (SD)	5.3 (1.6)	5.3 (3.6)	.121
Avg Tail Gate (#)	Mean (SD)	6.1 (9.0)	3.6 (6.7)	.355
Time Over Speed (second)	Mean (SD)	4.0 (4.2)	2.5 (3.6)	.454
Dist Over Speed (%)	Mean (SD)	7.5 (7.8)	4.5 (6.7)	.321
Time Excess (%)	Mean (SD)	0.4 (0.7)	0.2 (0.4)	.767
Dist Excess (%)	Mean (SD)	0.6 (1.3)	0.4 (0.6)	.762
Collisions (#)	Mean (SD)	0.8 (0.8)	1.3 (1.2)	.305
Signal Light Infr (#)	Mean (SD)	0.4 (0.7)	0.7 (0.6)	.140
Stops Red (#)	Mean (SD)	3.3 (1.0)	3.1 (0.8)	.323
Words Correct (#)	Mean (SD)	5.7 (0.6)	5.0 (1.8)	.298
Words Incorrect (#)	Mean (SD)	0.3 (0.6)	0.5 (1.0)	.570
Avg Word Response (#)	Mean (SD)	1.2 (0.3)	1.1 (0.6)	.452
Word Response Dev (#)	Mean (SD)	0.5 (0.4)	0.5 (0.3)	.800
VDA Correct (#)	Mean (SD)	2.9 (0.3)	2.5 (1.0)	.196
VDA Missed (#)	Mean (SD)	0.1 (0.3)	0.2 (0.6)	.265
Avg VDA Response (seconds)	Mean (SD)	2.4 (0.5)	2.9 (0.3)	.036
VDA Response Dev	Mean (SD)	0.5 (0.3)	0.4 (0.3)	.924
AQ Correct (#)	Mean (SD)	1.9 (1.0)	1.8 (1.2)	.994
AQ Missed (#)	Mean (SD)	1.0 (1.0)	0.9 (1.1)	.855
Avg AQ Response	Mean (SD)	0.6 (0.7)	0.4 (0.4)	.219
AQ Response Dev	Mean (SD)	0.3 (0.4)	0.2 (0.3)	.964
Avg Tailgates (#)	2 or more	2 (6.5%)	0 (0%)	.537
Tailgate Dev (#)	-	-	-	.908
Excess Speed (#)	3 or more	1 (3.2%)	0 (0%)	.969
Off Road Accidents (#)	2 or more	1 (3.2%)	0 (0%)	.931
Ped Collisions (#)	total	21 (67.7%)	4 (30.8%)	.076
Total Collisions (#)	Total (%)	24 (25.8%)	6 (15.4%)	.035
Stop Sign Infractions (#)	Total (%)	21 (67.7%)	4 (30.8%)	.850
Map 1 performance (#)	Correct (%)	5 (16.1%)	5 (38.5%)	.193
Map 2 performance (#)	Correct (%)	5 (16.1%)	1 (7.7%)	.641
Map 3 performance (#)	Correct (%)	9 (29%)	9 (69.2%)	.046
Total Map performance $(#)$	Correct (%)	19 (20.4%)	15 (38.5%)	.020
Words correct (#)	Total (%)	31 (100%)	13 (100%)	.00
VDA correct (#)	Total (%)	31 (100%)	13 (100%)	1.00
AQ correct (#)	Total (%)	30 (96.8%)	13 (100%)	.781

may assist with decisions regarding driving capacity of cirrhotic patients remains an unknown possibility. More research is warranted in this arena.

As a small, unmatched pilot study, our findings have limitations that need to be acknowledged. For example, cirrhotic participants tended to be less educated and were more likely to be men than were members of the healthy group. Also, the healthy volunteers were mostly colleagues at our institution, which may have skewed the average education level compared with that of our cirrhotic participants. Although differences in age, education, and sex

did not reach significance, a combination of these differences may have influenced the ability of the cirrhotic cohort to perform a computerized audiovisual task, such as driving simulation. In fact, several studies that compared driving simulator performance of young adults to that of older

HEADS score	Probability of cognitive impairment		
0	0.00	-	
1	0.00		
2	0.00		
3	0.01		
4	0.02		
5	0.08		
6	0.19		
7	0.42		
8	0.71		
9	0.89		

Table 5. Estimated probability for being cognitively impaired for a HEADS score

adults have shown a significantly decreased ability to divide attention in the older age groups.<sup>14,15</sup> In our study, the influence of age was apparent in lane tracking and in the accuracy of visual analysis. Our data also suggested that difficulty in integrating responses could be a determinant of poor dual-task performance in older subjects. However, a recent report showed that driving performance across three age groups (21–66 years) was relatively stable with regard to attention and ability to be distracted.<sup>16</sup> Of note, in our study, a key difference was that older drivers traveled at lower mean speeds than did younger drivers. We also noted lower mean speeds in the cirrhotic group as assessed by longer total run times. Whether lower speed was a factor of age, education level, sex, liver disease, or a combination of all variables will require further study with larger sample sizes matched for age, sex, and education level.

In summary, HEADS is a computerized driving simulation intended for the quantitative assessment of mild hepatic encephalopathy. How this new tool will



Fig 2. Receiver Operater Curve (ROC) of HEADS Score

...based on our preliminary data, the HEADS scoring system may some day afford the clinician with a simple and practical approach to detect and measure cognitive impairment in cirrhotic patients.

complement current neuropsychological testing routines in the evaluation of cirrhotic patients remains to be seen. However, based on our preliminary data, the HEADS scoring system may some day afford the clinician with a simple and practical approach to detect and measure cognitive impairment in cirrhotic patients. The HEADS system may also be useful in the evaluation of new therapies for the treatment of mild hepatic encephalopathy.

#### REFERENCES

- Groeneweg M, Quero JC, De Bruijn I, et al. Subclinical hepatic encephalopathy impairs daily functioning. *Hepatology*. 1998;28:45–49.
- Bajaj JS, Etemadian A, Hafeezullah M, Saeian K. Testing for minimal hepatic encephalopathy in the United States: an AASLD survey. *Hepatology*. 2007;45:833–834.
- Wein C, Koch H, Popp B, Oehler G, Schauder P. Minimal hepatic encephalopathy impairs fitness to drive. *Hepatology*. 2004;39: 739–745.
- Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT. Hepatic encephalopathy—definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. *Hepatology*. 200;35:716–721.
- Kale RA, Gupta RK, Saraswat VA, et al. Demonstration of interstitial cerebral edema with diffusion tensor MR imaging in type C hepatic encephalopathy. *Hepatology*. 2006; 43:698–706.
- Hassanein TR, Hilsabeck T, Marcott M, Carlson WP. Driving performance in patients with chronic liver disease. *Hepatology*. 2003;abstract 419A.

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- Conn HO, Leevy CM, Vlahcevic ZR, et al. Comparison of lactulose and neomycin in the treatment of chronic portal-systemic encephalopathy. A double blind controlled trial. *Gastroenterology*. 1977;72:573–583.
- Quero JC, Hartmann IJ, Meulstee J, Hop WC, Schalm SW. The diagnosis of subclinical hepatic encephalopathy in patients with cirrhosis using neuropsychological tests and automated electroencephalogram analysis. *Hepatology.* 1996;24:556–560.
- Jover R, Company L, Gutierrez A, et al. Minimal hepatic encephalopathy and extrapyramidal signs in patients with cirrhosis. *Am J Gastroenterol.* 2003;98:1599–604.
- Dhiman RK, Sawhney MS, Chawla YK, Das G, Ram S, Dilawari JB. Efficacy of lactulose in cirrhotic patients with subclinical hepatic encephalopathy. *Dig Dis Sci.* 2000;45: 1549–1552.
- 11. Demetriou AA, Brown RS Jr., Busuttil RW, et al. Prospective, randomized, multicenter, controlled trial of a bioartificial liver in treating

acute liver failure. *Ann Surg.* 2004;239: 660–667.

- Baskin-Bey ES, Kremers W, Nyberg SL. Improving utilization of deceased donor kidneys by matching recipient and graft survival. *Transplantation*. 2006;82:10–14.
- Watanabe A, Tuchida T, Yata Y, Kuwabara Y. Evaluation of neuropsychological function in patients with liver cirrhosis with special reference to their driving ability. *Metab Brain Dis.* 1995;10:239–248.
- Brouwer WH, Waterink W, Van Wolffelaar PC, Rothengatter T. Divided attention in experienced young and older drivers: lane tracking and visual analysis in a dynamic driving simulator. *Hum Factors*. 1991;33: 573–582.
- Chaparro A, Wood JM, Carberry T. Effects of age and auditory and visual dual tasks on closed-road driving performance. *Optom Vis Sci.* 2005;82:747–754.
- Horberry T, Anderson J, Regan MA, Triggs TJ, Brown J. Driver distraction: the effects of

concurrent in-vehicle tasks, road environment complexity and age on driving performance. *Accid Anal Prev.* 2006;38:185–191.

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