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A Low-Cost, User-Friendly Electroencephalographic Recording System for the Assessment of Hepatic Encephalopathy

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Electroencephalography (EEG) is useful to objectively diagnose/grade hepatic encephalopathy (HE) across its spectrum of severity. However, it requires expensive equipment, and hepatogastroenterologists are generally unfamiliar with its acquisition/interpretation. Recent technological advances have led to the development of low-cost, user-friendly EEG systems, allowing EEG acquisition also in settings with limited neurophysiological experience. The aim of this study was to assess the relationship between EEG parameters obtained from a standard-EEG system and from a commercial, low-cost wireless headset (light-EEG) in patients with cirrhosis and varying degrees of HE. Seventy-two patients (58 males, 61 ± 9 years) underwent clinical evaluation, the Psychometric Hepatic Encephalopathy Score (PHES), and EEG recording with both systems. Automated EEG parameters were calculated on two derivations. Strong correlations were observed between automated parameters obtained from the two EEG systems. Bland and Altman analysis indicated that the two systems provided comparable automated parameters, and agreement between classifications (normal versus abnormal EEG) based on standard-EEG and light-EEG was good ($0.6 < \kappa < 0.8$). Automated parameters such as the mean dominant frequency obtained from the light-EEG correlated significantly with the Model for End-Stage Liver Disease score ($r = -0.39$, $P < 0.05$), fasting venous ammonia levels ($r = -0.41$, $P < 0.01$), and PHES ($r = -0.49$, $P < 0.001$). Finally, significant differences in light-EEG parameters were observed in patients with varying degrees of HE. *Conclusion:* Reliable EEG parameters for HE diagnosing/grading can be obtained from a cheap, commercial, wireless headset; this may lead to more widespread use of this patient-independent tool both in routine liver practice and in the research setting. (HEPATOLOGY 2016;63:1651-1659)

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome caused by liver disease and/or portal-systemic shunting, which manifests as a wide spectrum of mental and motor dysfunction.

Patients with cirrhosis and HE exhibit electroencephalographic (EEG) alterations. These were first identified in 1950 by Foley and colleagues, who described high-voltage, slow waves in patients with hepatic coma.[1] A few years later, Parsons-Smith and colleagues reported that EEG alterations in patients with cirrhosis were related to the severity of overt HE (i.e., the more severe the clinical picture, the slower the EEG).[2] The same authors highlighted how mild EEG slowing could also be detected in patients without overt HE, thus already introducing the concept of latent or subclinical HE.[2] The visual classification of EEG changes proposed by Parsons-Smith and colleagues was descriptive in nature and thus prone to interobserver variability. In 1977, Conn and coworkers proposed a semiquantitative classification based

Abbreviations: EEG, electroencephalography; HE, hepatic encephalopathy; MDF, mean dominant frequency; MELD, Model for End-Stage Liver Disease; MPZS, mean PHES z score; PHES, Psychometric Hepatic Encephalopathy Score.

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on visual estimates of the slowing of the EEG.[3] This was later modified to automatically obtain a set of parameters defining the EEG frequency by means of an automated analysis of the digitized tracing (spectral analysis).[4] This classification has been proven to be more objective and more reliable compared to visual assessment.[5] In addition, it has been shown to hold prognostic value in relation to the occurrence of both HE and liver-related death.[6] Finally, recent research from our group has shown that the addition of an automated index of EEG frequency improves the prognostic value of the Model of End-Stage Liver Disease (MELD) score.[7] Despite these qualities, the EEG is not commonly used in clinical practice as it requires costly equipment (approximately $30,000) and a certain degree of expertise. In addition, hepatogastroenterologists are generally unfamiliar with both its acquisition and its interpretation.

Over the last few years, technological advances in the field of brain-computer interface have led to the development of novel EEG recording tools which are considerably cheaper (approximately $1,000) and more user-friendly. The aim of the present study was to compare automated indices obtained from one such wireless tool (light-EEG) and from a standard-EEG recording system, for purposes of HE diagnosis and quantification.

Patients and Methods

Seventy-two consecutive outpatients with cirrhosis were enrolled (58 men, age [mean ± standard deviation] 61 ± 9 years; Child class A 37%, B 54%, C 9%[8]; MELD 15 ± 5[9]; average fasting venous ammonia level 74 ± 42 μmol/L). The etiology of cirrhosis was chronic viral hepatitis, either B or C, in 43% of patients, alcohol misuse in 29%, mixed (viral hepatitis plus alcohol) in 20%, and nonalcoholic steatohepatitis/cryptogenic in the remaining 8%. Patients were excluded if they were actively misusing alcohol, had diagnosed or suspected cerebrovascular or cardiovascular disease, renal failure, significant neurological or psychiatric comorbidity or were taking psychoactive drugs.

One patient was studied on admission for an episode of grade III HE precipitated by constipation and then the following day, when the episode had started to resolve in response to treatment.

The study protocol was approved by the local Ethics and Research Committee and conducted according to the Declaration of Helsinki (Hong Kong amendment) and good clinical practice (European) guidelines.

NEUROPHYSIOLOGICAL ASSESSMENT

All patients underwent 10-minute, eyes-closed EEG recording with both the light-EEG and standard-EEG systems, in a condition of relaxed wakefulness and in a quiet room, first thing in the morning (08:30-09:00). Attention was paid to avoid somnolence. The light-EEG was always obtained first as it does not require conductive paste. This is needed for standard-EEG acquisition and once on the scalp/hair would compromise light-EEG acquisition.

Light-EEG Recording

This was recorded using the Emotiv EPOC 16-electrode cap (http://www.emotiv.com). The Emotiv EPOC is a wireless, noninvasive, portable, and reusable EEG system, marketed as a gaming device, and consists of a semirigid headset with 14 recording plus two reference electrodes (Fig. 1A,B). Each electrode contains a felt pad that is wetted with saline solution before being positioned on the semirigid plastic arms of the headset, at 10-10 International System positions [10] (Fig. 1C). The two electrodes, AF3 and AF4 (Fig. 1C), are positioned 4-6 cm above the eyebrows; the two reference electrodes (joint P4-right mastoid and joint P3-left mastoid) are located just above and behind the ears. Impedance is visually monitored using the Emotiv Control Panel software. Data are acquired at 2048 Hz using the

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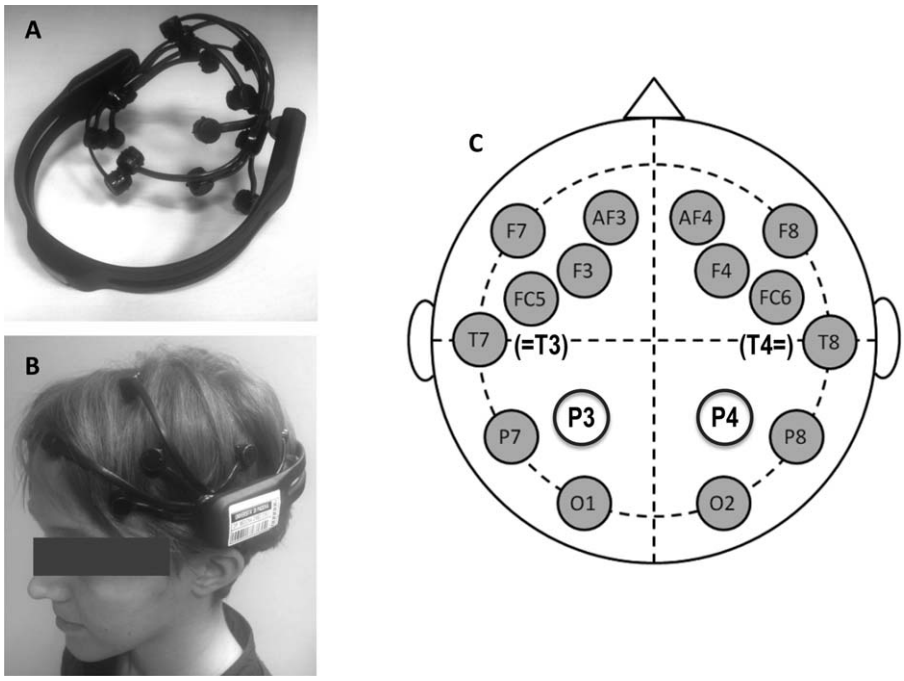


FIG. 1. The Emotiv EPOC 16-electrode cap off (A) and on a subject's head (B). Light-EEG scalp recording sites (C; gray circles), labeled according to the 10-10 system. The two white circles indicate the position of the 10-20 system standard-EEG biparietal electrodes, for comparative purposes. T3 and T4 (in parentheses) are the exact equivalents of T7 and T8 on the 10-20 labeling system. Therefore, standard-EEG P3-P4 ≅ light-EEG P7-P8; standard-EEG T3-O1 = light-EEG T7-O1; standard-EEG T4-O3 = light-EEG T8-O2. Abbreviations: AF, anterior frontal; F, frontal; O, occipital; P, parietal; T, temporal.

embedded 16-bit analog-to-digital converter and sent to a computer at 128 Hz sampling frequency per channel by Bluetooth. Data are bandpass-filtered offline in the 5-30 Hz range. Light-EEG recording requires 5 minutes for electrode preparation and placement plus 10-12 minutes for recording.

Standard-EEG Recording

Standard-EEG recording was obtained by Brainquick 3200 digital EEG equipment (Micromed, Italy). A 21-channel cap was used, and the electrodes were placed according to the 10-20 International System[11] (ground: Fpz, reference Oz). Prior to cap positioning, the scalp and hair were lightly cleaned with alcohol; conductive paste was injected into each electrode cup, and impedance was kept under 5 kΩ. Each channel had its own analog-to-digital converter, and signals were digitally filtered in the 1.6-70 Hz range. Sampling frequency was 256 Hz, 12-bit analog-to-digital conversion. Standard-EEG recording requires 10-15 minutes for electrode placement and impedance lowering plus 10-12 minutes for recording.

Spectral Analysis

One continuous 80-100 s period of EEG tracing from both recordings was selected manually by an operator (authors M.D.R., S.M.) for subsequent spectral analysis by fast Fourier transform; each selected section was qualified as artifact-free or as having features that could impinge on automated analysis. The most common such features are muscle artifact (high-frequency EEG artifact which derives from incomplete relaxation of muscles in the proximity of one or more electrodes: for example, teeth clenching/incomplete jaw relaxation can result in muscle artifact on anterior temporal electrodes, which are placed just behind the ears) and low power (i.e., EEG activity of very small amplitude, which may impinge on the quality of automated analysis). However, automated analysis was performed on all tracings, which were then treated both as a complete set (all EEGs) and as a smaller, artifact-free set (artifact-free EEGs). The following automated parameters were obtained: mean dominant frequency (MDF), which is an estimate of the background frequency of the EEG, and relative power of the spectral bands delta (1-3.5 Hz, very slow wake EEG activity), theta (4-7.5 Hz, slow wake EEG activity), alpha (8-13 Hz, normal wake EEG activity), and beta (13.5-26.5, fast wake EEG activity). The MDF, delta, and theta are all measures of EEG slowing and are used in combination to grade EEG alterations due to HE.[4,5] Theta activity increases in covert and mild overt HE and then decreases in severe overt HE (inverse U distribution), while delta starts increasing only in severe overt HE. Therefore, neither theta nor delta have a

linear relationship with HE severity, while MDF does. Thus, MDF is probably the single best summary index of EEG slowing in this context, albeit not very sensitive to the initial increase in theta activity.

Automated parameters were obtained on the derivations P3-P4 (biparietal),[5] T3-O1, and T4-O2 (temporal-occipital)[4] of the standard-EEG, as described.[5] Spectral parameters were also obtained on the derivations P7-P8 (biparietal), T3/T7-O1, and T4/T8-O2 (temporal-occipital) of the light-EEG (Fig. 1C).

The following comparisons were performed: standard-EEG temporal-occipital versus light-EEG temporal-occipital; standard-EEG biparietal versus light-EEG biparietal. In the light-EEG system the electrodes P3 and P4 are used as reference, together with the mastoids, and thus are not available for acquisition; P7 and P8 on the light-EEG are the closest to P3 and P4 on the standard-EEG (approximately 4 cm, depending on the size of the head; Fig. 1C). Given the spatial resolution of the EEG, standard-EEG P3-P4 and light-EEG P7-P8 can be considered comparable for purposes of frequency estimates (Fig. 1C).

The EEG was qualified as normal/abnormal according to Amodio and coworkers.[5] For this purpose, both the average of the temporal-occipital derivations[4,5] and the biparietal derivation were used and the pertinent thresholds applied.[5]

NEUROPSYCHOLOGICAL ASSESSMENT

Psychometric performance was assessed, under standardized conditions, immediately after EEG acquisition, using Number Connection Tests A and B as well as the Digit Symbol, Line Tracing, and Serial Dotting tests.[12] Results were scored in relation to age-adjusted and education-adjusted Italian norms.[13] Performance was classified as impaired if the sum of the standard deviations for the individual tests, referred to as the Psychometric Hepatic Encephalopathy Score (PHES), was ≤ -4[12,13]; the mean of the z scores for each subtest (MPZS)[13] was also used for purposes of correlation analysis as it is both a slightly more accurate (average z score rather than sum of the rounded z integers), symmetrically distributed and more continuous index.[13]

NEUROPSYCHIATRIC STATUS

Neuropsychiatric status on the day of study was classified as *unimpaired*: no clinical evidence of HE and normal PHES; *covert HE*: no obvious clinical abnormalities but abnormal PHES; *overt HE*: clinically evident neuropsychiatric disturbances ($\geq$grade 2 according to the West Haven criteria[3] applied by authors M.D.R., S.M., and P.Am., and/or asterixis[14]).

STATISTICAL ANALYSIS

Based on an expected average variation of MDF of 0.6 Hz, with a standard deviation of 1 Hz[15] and no expected variations in MDF differences in relation to EEG frequency (i.e., HE severity), it was calculated that 43 EEGs would be adequate for the purpose of MDF comparisons between standard-EEG and light-EEG. Agreement between spectral parameters obtained from the two EEG recording tools was assessed by the Bland and Altman method.[16] This compares a new measurement technique with an established one (with the aim of deciding whether they agree sufficiently for the new to replace the old) with an approach based on graphs and simple calculations.[16] Concordance between EEG classification (normal/abnormal) on light-EEG versus standard-EEG equipment was tested by Cohen's κ[17] and qualified as follows: $\kappa < 0$, no concordance; $0 < \kappa < 0.4$, poor; $0.4 < \kappa < 0.6$, sufficient; $0.6 < \kappa < 0.8$, good; $0.8 < \kappa < 1$ very good. Correlation analysis was performed by the Pearson r or Spearman ranks, as appropriate. Differences in spectral/psychometric parameters in different groups (normal/abnormal or varying degrees of HE) were performed by the Student t/Mann-Whitney U (two groups) or by analysis of variance (three groups, post hoc Tukey test). MDF, delta, and theta power were all included in the analysis; MDF was used where a summary index was needed for graphical representation or summary analyses.

Results

On the day of study, 33 (46%) patients were classified as neuropsychiatrically unimpaired, 18 (25%) as having covert HE (abnormal PHES performance), and 21 (29%) as having overt HE (Table 1). Eight standard-EEG derivations (8/72*3; 4%) were qualified as being inadequate for the purposes of spectral analysis (three because of low power and five because of muscle artifact). Twenty light-EEG derivations (20/72*3; 9%) were qualified as being inadequate for purposes of spectral analysis (three because of low power, two because of background electrical noise, and 15 because of muscle artifact). Therefore, the reduced, artifact-free sample included 44 matching tracings for

TABLE 1. Characteristics of the Patient Population

	Entire Population (n = 72)	Unimpaired (n = 33)	Covert HE (n = 18)	Overt HE (n = 21)
Age (years)	61 ± 9	59 ± 9	61 ± 11	64 ± 7
Males/females	58/16	29/4	13/5	14/7†‡
MELD score	15 ± 5	13 ± 5	13 ± 2	18 ± 5‡
NH4, μmol/L (% abnormal)	74 ± 42	71 ± 39 (71%)	56 ± 19 (93%)	99 ± 57 (100%)
PHES (% abnormal)	−3.9 ± 4.9	−0.2 ± 1.5 (0%)	−5.7 ± 2.1 (100%)	−10.2 ± 5.4 (95%)*

*Of patients with overt HE, 29% were unable to complete all or some of the PHES subtests; patients with overt HE and normal PHES performance were qualified as having overt HE because of the presence of asterixis (see Vilstrup et al.)[14] despite being orientated in space and time and able to produce a near-normal PHES performance.
Overt HE versus unimpaired †$P < 0.001$; overt HE versus covert HE ‡$P < 0.05$.

all derivations (58 for T3-O1, 54 for T4-O2 [49 for both temporal-occipital derivations], and 62 for P3-P4/P7-P8).

All automated parameters obtained from the two EEG systems were significantly correlated; correlations were generally stronger when only the artifact-free EEGs were taken into consideration (Table 2).

Bland and Altman analysis for the complete sample (all EEGs) is presented in Table 3. The analysis showed comparable results for the light-EEG and standard-EEG, with acceptable average differences and acceptable ranges of oscillation (Table 3 and Fig. 2). Averages were even closer to zero and differences generally smaller when only the artifact-free EEGs were taken into consideration. Significant correlations were observed between the difference and the average theta power in the complete sample ($r_{T4\text{-}O2} = 0.29$, $P < 0.01$; $r_{P3P4/P7P8} = 0.29$, $P < 0.01$), indicating a small, systematic difference between light-EEG and standard-EEG estimates, the former underestimating the relative theta power compared to the latter and the difference being higher for higher theta values. This was confirmed when only the artifact-free EEGs were taken into consideration. Significant correlations were observed between the difference and the average delta power in the complete sample ($r_{P3P4/P7P8} = -0.32$, $P < 0.01$), indicating a small, systematic difference between light-EEG and standard-EEG estimates, the former underestimating the relative delta power compared to the latter and the difference being higher for higher delta values. This was confirmed when only the artifact-free EEGs were taken into consideration. No significant correlations between the differences and the average of the MDF were detected on any derivation.

On the complete sample, 43 patients had abnormal standard-EEG on the temporal-occipital derivation and 36 on the biparietal derivation; 37 patients had abnormal light-EEG on the temporal-occipital derivation and 34 on the biparietal derivation. Agreement between classifications (normal versus abnormal EEG; standard-EEG used as a gold standard) based on standard-EEG and light-EEG was good ($0.6 < \kappa < 0.8$) on both the temporal-occipital derivation ($\chi^2 = 27$, $P = 0.0001$; Cohen's $\kappa = 0.61$; four false positives and 10 false negatives) and the bi-parietal derivation ($\chi^2 = 27$, $P = 0.0001$; Cohen's $\kappa = 0.61$; six false positives and eight false negatives).

When only the artifact-free EEGs were taken into consideration, 27 patients had abnormal standard-EEG on the temporal-occipital derivation and 29 on the biparietal derivation; 23 patients had abnormal light-EEG on the temporal-occipital derivation and 31 on the biparietal derivation. Agreement between classifications was good ($0.6 < \kappa < 0.8$) on both the temporal-occipital derivation ($\chi^2 = 23$, $P = 0.0001$; Cohen's $\kappa = 0.68$; six false positives and two false

TABLE 2. Correlations Between the Automated Parameters Derived From Standard-EEG and Light-EEG

EEG Derivation	Automated Index	All EEGs		Artifact-Free EEGs	
		R/r	*p*	*R/r*	*p*
P3-P4/P7-P8	MDF	0.61	<0.0001	0.73	<0.0001
	Theta %	0.76	<0.0001	0.78	<0.0001
	Delta %	0.77	<0.0001	0.79	<0.0001
T3-O1	MDF	0.53	<0.0001	0.72	<0.0001
	Theta %	0.81	<0.0001	0.90	<0.0001
	Delta %	0.70	<0.0001	0.74	<0.0001
T4-O2	MDF	0.41	<0.001	0.52	<0.0001
	Theta %	0.83	<0.0001	0.84	<0.0001
	Delta%	0.47	<0.0001	0.44	<0.01

R/r (Spearman ranks/Pearson *r*) refers to the correlation between light and standard EEG. MDF, delta, and theta are all measures of EEG slowing; and they are used in combination to grade EEG alterations due to HE. Theta (slow) activity increases in covert and mild overt HE and then decreases in severe overt HE (inverse U distribution), while delta (very slow) starts increasing only in severe overt HE. The MDF is probably the single best summary index of EEG slowing in this context, albeit not very sensitive to the initial increase in theta activity, and it has a linear relationship with HE severity.

TABLE 3. Bland and Altman Analysis of Automated Parameters Derived From Standard-EEG and Light-EEG, Complete Sample

EEG Derivation	Spectral Index	Mean of the Differences (95% CI) (Standard; Light)	Limits of Agreement	
			Lower	Upper
P3-P4/P7-P8	MDF (Hz)	−0.68 (−4.24; +2.87)	−1.21	−0.15
	Theta (%)	+4.21 (−19.7; +28.13)	+0.64	+7.78
	Delta (%)	−3.5 (−19.7; +12.3)	−5.83	−1.19
T3-O1	MDF (Hz)	−0.44 (−4.85; +3.97)	−1.1	+0.21
	Theta (%)	+4.27 (−19.22; +27.77)	+0.77	+7.78
	Delta (%)	−3.46 (−23.61; 16.68)	−6.47	−0.45
T4-O2	MDF (Hz)	−0.54 (−4.86; +3.79)	−1.18	+0.11
	Theta (%)	+5.94 (−16.08; +27.95)	+2.65	+9.22
	Delta (%)	−3.64 (−27.70; +20.42)	−7.2	−0.04

negatives) and the biparietal derivation ($\chi^2 = 29$, $P = 0.0001$; Cohen's $\kappa = 0.62$; six false positives and four false negatives).

Spectral parameters obtained from the light-EEG correlated significantly with both the MELD score (i.e., $MDF_{P3P4/P7P8}$ $r = -0.46$, $P < 0.01$; $theta\%_{P3P4/P7P8}$ $r = 0.36$, $P < 0.05$; $delta\%_{P3P4/P7P8}$ $r = 0.31$, $P < 0.05$) and fasting, venous ammonia levels (i.e., $MDF_{P3P4/P7P8}$ $r = -0.34$, $P < 0.05$; $theta\%_{P3P4/P7P8}$ $r = 0.26$, $0.05 < P < 0.1$; $delta\%_{P3P4/P7P8}$ $r = 0.33$, $P < 0.05$) (Fig. 3A-C). Significant differences were observed in light-EEG automated parameters between patients with varying severity of HE (Fig. 4). Similarly, patients with abnormal light-EEG had significantly worse psychometric performance than their counterparts qualified as normal (MPZS -1.51 ± 1.59 versus -0.64 ± 1.25, $P < 0.05$ on the temporal-occipital derivation; -1.59 ± 1.54 versus -0.61 ± 1.27 on the biparietal derivation). Finally, significant correlations were observed between light-EEG automated parameters and PHES performance (i.e., MDF_{P7-P8} versus MPZS $r = -0.43$, $P < 0.01$). All subtests of the PHES correlated significantly with light-EEG automated indices. Correlations were generally more consistent and stronger for the MDF (as opposed to theta and delta) and for Number Connection Test A (as opposed to the remaining four tests).

The time course of clinical status, ammonia levels, and psychometric and light-EEG indices in the patient who was studied twice are presented in Fig. 5.

Discussion

The light-EEG system tested in this study produced automated index estimates which were comparable to those of the standard-EEG and significantly correlated with both indices of hepatic and neuropsychiatric dysfunction.

Differences in spectral parameters obtained from the standard-EEG and the light-EEG were negligible, and rates of misclassification were acceptable. Discrepancies in the complete sample were mostly due to the presence of artifact in either the standard-EEG or the light-EEG. Discrepancies in the artifact-free EEGs were mostly due to near-threshold values. For example, if the threshold for abnormal theta is 35% and theta oscillates around 35, a value of 34 on light-EEG and 36 on standard-EEG would result in the record being qualified as normal on light-EEG and abnormal on standard-EEG. It is also true that a patient with a theta of approximately 35% is genuinely on the very border between a normal and an

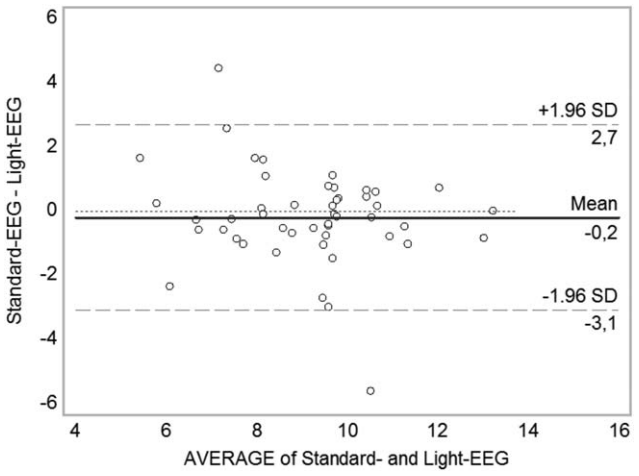


FIG. 2. The Bland and Altman plot of the biparietal MDF: averages of the value obtained from the standard-EEG and light-EEG (*x* axis) plotted against the differences of the value obtained from the standard-EEG and light-EEG (*y* axis). As can be observed from the plot, the differences between the two estimates were, as a mean, close to zero (mean = −0.2 Hz on the plot), and oscillations of up to approximately 3 Hz in each direction (±1.96 standard deviation) were observed, with no systematic error (i.e., no significant linear correlation between averages and differences). Abbreviation: SD, standard deviation.

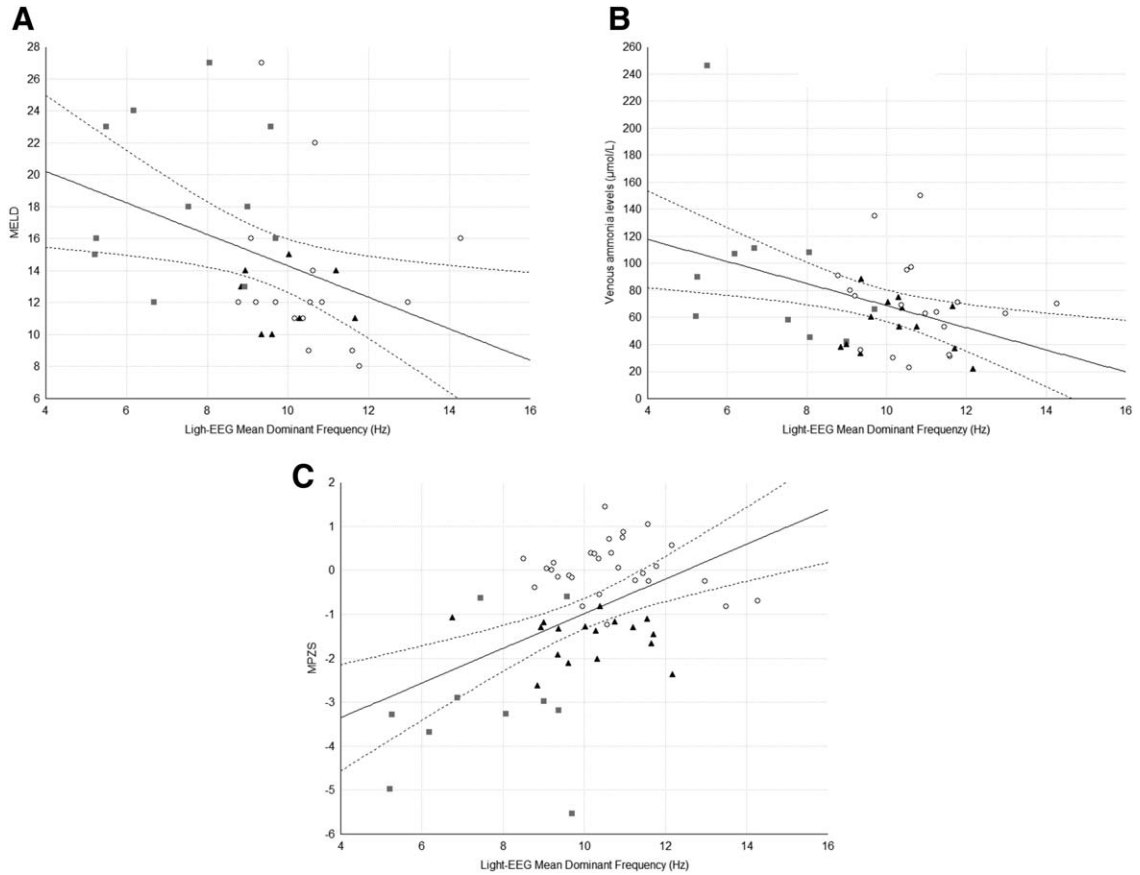


FIG. 3. Correlation plots for light-EEG biparietal MDF and MELD (A; $r = -0.39$, $P < 0.05$); fasting, venous ammonia levels (B; $r = -0.41$, $P < 0.01$) and the mean of the z scores for each of the PHES subtests (MPZS) (C; $r = 0.49$, $P < 0.001$). The neuropsychiatric status of each patient has also been highlighted, with light gray squares being patients with overt HE, dark gray triangles being patients with covert HE, and empty circles being unimpaired patients.

abnormal EEG. The observed differences between standard-EEG and light-EEG appear to be even more acceptable if we consider that comparisons were made between EEG tracings which were recorded not only with different equipment but also at slightly different parietal scalp sites (P3-P4 versus P7-P8) and at slightly different times, albeit within the space of 20-30 minutes. Small changes are known to occur over time even within the same EEG, and these could easily explain misclassification, especially if automated parameters are close to the abnormality thresholds,[15] as explained in the example above. In addition, it should be observed that in the whole sample, in which all tracings were included and limited attention was paid to artifact, agreement was still good. While patient satisfaction was not formally assessed, light-EEG recording, which does not require the use of conductive paste and allows for faster impedance lowering, seemed to be better tolerated.

A higher proportion of derivations from the light-EEG were discarded because of artifact, and this could be due to imperfect electrode positioning and/or some degree of instability of the system. However, it should also be highlighted that in our laboratory we have been using the standard-EEG for decades, while we were substantially new to the light-EEG when the study started. It is therefore possible that the observed results are related, at least to some extent, to our own learning curve and that fewer light-EEG tracings will be discarded in the future. The presence of some degree of muscle artifact, which was particularly common on the temporal-occipital derivations of the light-EEG, may also contribute to the small but systematic underestimation of the theta power. This is because muscle artifact results in artificial, overestimated fast (beta) EEG activity and, in turn, in underestimation of all the remaining, relative activities contributing to the spectrum.[18]

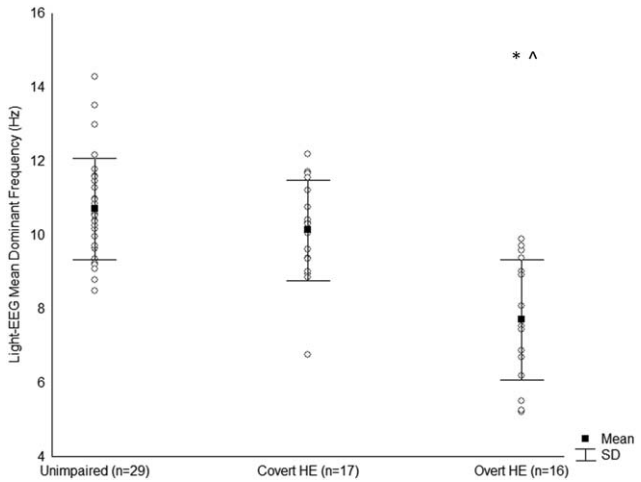


FIG. 4. MDF values (plus mean and standard deviation, by group) obtained from spectral analysis of the biparietal derivation of the light-EEG system in patients with varying degrees of HE. Overt HE versus unimpaired $^{*}P < 0.001$; overt HE versus covert HE $^{\wedge}P < 0.001$. Abbreviation: SD, standard deviation.

Automated parameters derived from the light-EEG system were shown to correlate with the MELD score, fasting ammonia levels, and the average *z* score of the PHES battery, thus confirming that such parameters reflect neuropsychiatric dysfunction caused by liver disease.[14,19] Similarly, automated parameters derived from the light-EEG system mirrored the severity of HE measured by clinical (overt versus no overt) and psychometric tools (abnormal versus normal PHES). In addition, such parameters reflected changes in neuropsychiatric performance and ammonia levels in the patient who was studied twice, on admission and 24 hours after the institution of treatment for an episode of precipitated, severe overt HE. All these results suggest that spectral parameters derived from the light-EEG are reliable for purposes of HE diagnosis and grading.[14,19] These findings obviously need confirmation in similar studies, also in patient populations which are more even in terms of sex and etiology of cirrhosis.

The EEG is the only patient-independent, quantitative tool for HE assessment.[20] All other neuropsychological and psychophysical tools can be affected, to varying extents, by the patients' compliance and by their attitude toward the test, the diagnosis of cirrhosis or HE, and the transplantation selection procedures.[21,22] In addition, several such tests can only be used if the patient is well enough and cooperative enough. In contrast, EEG acquisition requires no cooperation. The EEG has been shown to hold prognostic value in relation to the occurrence of both HE and liver-related death.[6] More recently, it has also been shown that the addition of an automated index of EEG slowing (MDF) improves the prognostic value of MELD at both 12 and 18 months.[7] The EEG is

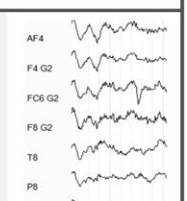
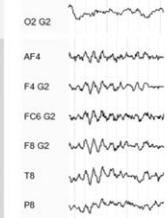
Day	Ammonia (μmol/L)	West-Haven Grade	PHES	Light EEG		
1	90	III	-13	MDF (Hz)	4.6	
				Delta (%)	51	
				Theta (%)	37	
2	67	II	-9	MDF (Hz)	6.7	
				Delta (%)	24	
				Theta (%)	42	

FIG. 5. Laboratory, clinical, psychometric, and automated light-EEG indices in a 63-year-old male patient (MELD 16) admitted for grade III, precipitated overt HE and reevaluated on the following day, when the episode had started to resolve. Light-EEG reflected the decrease in ammonia and the improvement in clinical/psychometric performance both on automated (MDF, delta, and theta) and on visual inspection of approximately 2 seconds of EEG recording (extreme right). On day 1, the tracing was dominated by large delta waves (very slow EEG activity), while on day 2 the tracing was less slow, albeit still abnormal, and dominated by theta waves (slow EEG activity).

also largely operator-independent, although selection of an artifact-free section for automated analysis has been, so far, performed manually (i.e., an operator visually analyzes the EEG and chooses the section). This part of the operation may also be amenable to full automation, and research efforts in this direction would certainly be useful. The slowing observed in the EEG is a marker of pathological changes in oscillatory brain activity, which extend across different subsystems of the brain and have been confirmed across different frequency bands, affecting, for example, cortical-muscle coherence (please refer to Butz et al.[23] for a review). Despite all these advantages, the EEG is not widely used, most likely in relation to high costs and the degree of expertise required. The light-EEG tool presented in this study and other, similar tools, which are available on the market for both leisure and medical purposes, may really help overcome such barriers. Tailor-made algorithms for immediate calculation of automated indices with an HE-specific output (MDF, delta, theta, and the MELD-EEG [http://www.rad.unipd.it/cirrhosis/index.php], as routinely in use in our department) could be easily made available, or even added to each specific light-EEG software. Such technological development would be easily obtained and most likely rewarding.

In conclusion, reliable EEG parameters for purposes of HE diagnosis and grading can be obtained from a cheap, commercial, wireless headset. This will hopefully lead to more widespread use of the EEG both in routine liver practice and in the research setting.

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