Dynamic posturography findings among patients with liver cirrhosis in Egypt

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Background
Liver cirrhosis is a condition that destroys the normal function of the liver, leading to hepatic encephalopathy, which is associated with impairment in postural control and disturbance in balance.

Aim of the study
The aim of this study was to detect the disturbances in balance and postural control because of hepatic encephalopathy as a result of liver cirrhosis using dynamic posturography.

Participants and methods
Individuals were divided into two groups: 45 patients with liver cirrhosis and 45 controls. Both groups underwent dynamic posturography to evaluate balance control, number connection test-type A, line tracing test, and serum ammonia (NH_3) level to assess encephalopathy.

Results
Dynamic posturography findings were significantly weaker in patients with liver cirrhosis than in the controls. They were also weaker in patients with high NH_3 than in patients with low NH_3. There were significant negative correlations between dynamic posturography findings and number connection test-type A, line tracing test, and NH_3 levels.

Conclusion
Hepatic encephalopathy because if liver cirrhosis affects balance control and the degree of affection is related to the degree of encephalopathy.

Keywords:
dynamic posturography, hepatic encephalopathy, liver cirrhosis

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Introduction

There are different etiologies for liver cirrhosis, but the most common causes are hepatitis B virus (HBV), hepatitis C virus (HCV), and obesity, which is associated with nonalcoholic fatty liver disease [1]. Egypt has the highest prevalence of adult HCV infection in the world, affecting an average of 15–25% of the population in rural communities [2]. Hepatic encephalopathy (HE) is a complication of advanced liver disease. The pathogenesis of HE is still unclear, but hyperammonemia because of increased production of ammonia (NH_3) in the gut and/or impaired removal by the impaired liver is considered to be the leading cause. Other possible mechanisms of HE include increase in levels of inhibitory neurotransmitter GABA, increase in brain levels of natural central benzodiazepine receptor agonists, and increased release of neurosteroids from astrocytes secondary to an increased NH_3 level. HE presents with a wide range of neuropsychiatric disturbances such as impaired motor function and asterixis, altered sleeping patterns, reduced state of consciousness, impaired intellectual abilities, and personality changes [3]. The presence of minimal HE has a negative effect on patients' daily activities because of psychomotor deficits, but it cannot be detected by a global clinical examination and requires specific neuropsychological and neurophysiological tests [4]. Impairment in postural control has been repeatedly suggested in the literature as one of the possible symptoms of HE, but so far, it has not been quantified objectively in these patients [5]. Computerized dynamic posturography is used to assess changes in body position when maintaining dynamic balance by eliminating or sway-referencing visual surrounds or conflicting somatosensory input by using a swaying support surface. After reviewing the literature, there was only one study by Schmid *et al.* [6] that used platform posturography to assess postural control in patients with liver cirrhosis of various etiologies [6]. Psychometric tests and number connection tests (NCTs) A and B are used to assess the presence of minimal HE [7]. However, postural control in cirrhotic patients has not yet been investigated in detail. Hence, the aim of this study was to detect the disturbances in balance and postural control because of HE as a result of liver cirrhosis, using dynamic posturography, and to assess the use of dynamic posturography as a possible tool to identify the early effects on balance among patients with liver cirrhosis.

Participants and methods

Participants

This was a case–control study. A total of 45 patients with liver cirrhosis were selected randomly from patients who were admitted to the Kasr Al Ainy internal medicine hospital or patients referred to the Kasr Al Ainy internal medicine outpatient clinic during the period from November 2009 to August 2010. Cirrhosis was diagnosed histologically or on a clinical basis through laboratory tests and sonographic examination. They were referred to the audiology unit for balance assessment using computerized dynamic posturography after a neurological evaluation was performed for the patient group to exclude other neurological disorders. Exclusion criteria were physical inability to undergo posturography (inability to stand or walk), overt or anamnestic neurological diseases (except HE) such as Parkinson's disease, history of vestibular lesions, cerebrovascular stroke, polyneuropathy, and paresis of the lower limbs. Similarly, patients who could not co-operate, those with obvious recent alcohol abuse before the investigation, and those with ophthalmologic disorders such as uncorrectable severe reduction of visual acuity or double vision were also excluded.

A total of 45 age-matched and sex-matched normal individuals without evidence of acute or chronic liver diseases served as controls.

Before this study, consent and approval to provide samples and to perform dynamic posturography tests was obtained from each participant after they were provided with an explanation of the aim and importance of the study. Strict confidentiality was maintained throughout sample collection, coding, testing, and recording of the results. Individuals were allowed to obtain copies of their results.

Methods

All patients were subjected to complete assessment of history, a thorough physical examination, and the following laboratory test measurements: serum albumin, total bilirubin, serum NH_3 concentration, HCV antibody (anti-HCV), hepatitis B surface antigen, HCV-RNA using quantitative PCR, circulating autoantibodies (ANA, ASMA), and abdominal ultrasonography.

Measurements

Computerized dynamic posturography was performed using the Neurocom Smart Equi Test Balance Master (NeuroCom International Inc., Clackamas, Oregon, USA). During the sensory organization test (SOT) procedure, patients were required to stand on a pressure sensitive, dynamic tilted force plate facing a sway-referenced visual surround, instructed and strapped into a safety harness to prevent injury in the event of a loss of balance. The SOT comprised three 20 s trials for each of the six conditions representing different aspects of balance. SOT1 – eyes open, fixed surface and visual surrounds; SOT2 – eyes closed, fixed surface; SOT3 – eyes open fixed surface, sway-referenced visual surround; SOT4 – eyes open, sway-referenced surface, fixed visual surround; SOT5 – eyes closed, sway-referenced surface; and SOT6 – eyes open, sway-referenced surface and visual surround. For each single test as well as for the composite performance, an equilibrium score was computed. The score was 100 for no sway at all, decreasing with increasing sway range during the 20 s measurement time. The patients were fitted with a safety harness and properly aligned on the force plate and instructed before testing [8].

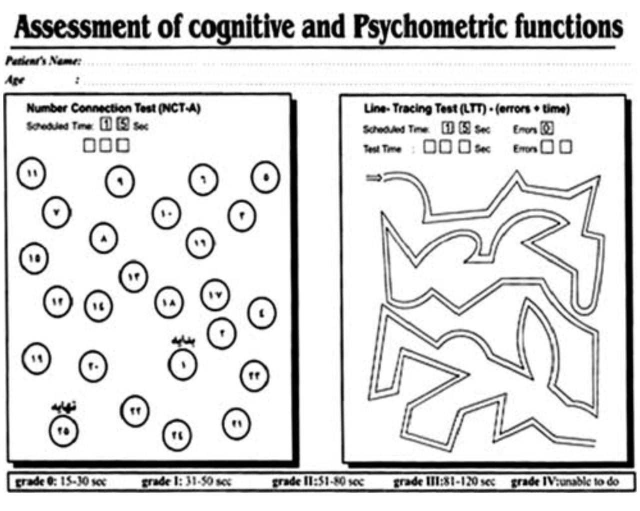
Psychometric testing

NCT-A and line tracing test (LTT) were performed to assess the presence of HE. Deviation of the test results from those found in an age-matched control group by 2 SD was considered abnormal. The NCT versions used in the study are shown in Fig. 1. In the NCT-A, the individual had to connect a sequence of scattered circles numbered 1, 2, 3…25 (note in Arabic letters) as quickly as possible. In the LTT, the individual had to trace a line run in a track as shown in Fig. 1. As recommended, NCT-A and LTT were performed consecutively, with the real test procedure being preceded by a test run using a training version. This test run provided the opportunity to familiarize the individuals with the test procedure. It also reduced the training effect, which might falsify the results in follow-up examinations [9].

Statistical analysis

Data obtained from the study were coded and entered using the statistical package SPSS version 16 (SPSS Inc., Chicago, Illinois, USA). The mean values and SD were then estimated for quantitative variables, and as for the qualitative variables, the frequency distribution was calculated. Comparisons between the exposed and the control groups were made using the independent-sample t-test. The correlations between individual variables were calculated using Pearson's correlation coefficient. P-values less than 0.05 were considered statistically significant.

Figure 1



Assessment of cognitive and psychometric functions.

Results

A total of 45 patients with liver cirrhosis were investigated in this study and 45 normal individuals served as controls. According to the etiology of cirrhosis, 87% of patients had HCV ($n=39$), 11% had HBV ($n=5$), and 2% had steatohepatitis ($n=1$). Different characteristics of the patient and the control groups are presented in Table 1. On comparing the patient group and the control group with respect to the results of dynamic posturography, there were statistically significant weaker performances in the patient group in SOT1 with P value less than 0.05 and SOT2, SOT3, SOT5, SOT6, and CS with P value of 0.001, whereas the difference between the two groups was not statistically significant in SOT4 Table 2.

According to the level of blood NH_3, the patient group was divided into two groups, group I included patients with high NH_3 (≥ 50, $n=24$) and group II included patients with low NH_3 (<50, $n=21$). There were statistically significant weaker performances in SOT1, SOT3, SOT4, and SOT5 ($P<0.05$), and SOT2, SOT6, and CS ($P=0.001$, Table 3) in group I compared with group II.

The patient group was divided into three groups according to the Child–Pugh score (Child–Pugh class A = 20, B = 11, and C = 14, Table 4). Patients with Child–Pugh classB had significantly weaker performances in SOT1, SOT2, SOT4, SOT6, and CS ($P<0.05$, Table 4), compared with Child–Pugh class A (Table 4).

Table 1 Characterization of the groups studied

	Patients (n=45)	Controls (n=45)	P value
Age (years)	50.46 ± 9.11	48.93 ± 8.12	0.302
Sex (M/F)	30/15	33/12	0.490
Albumin (g/dl)	2.58 ± 0.45	3.48 ± 0.34	0.034*
Bilirubin (mg/dl)	2.1 ± 0.79	0.50 ± 0.3	0.001*
NCT-A (s)	77.60 ± 21.72	16.75 ± 5.35	0.0001*
LTT	96.44 ± 20.44	33.73 ± 7.56	0.0005*
NH_3	77.06 ± 18.55	47.44 ± 10.05	0.001*

LTT, line tracing test; NCT-A, number connection test-type A; NH_3, ammonia.
*$P<0.05$ is statistically significant.

Table 2 *t*-Test results of SOT findings between the patient and the control group

	Mean ± SD		
	Patients (n=45)	Controls (n=45)	P value
SOT1	91.50 ± 2.77	92.92 ± 2.33	0.010*
SOT2	87.38 ± 4.59	90.24 ± 2.16	0.001*
SOT3	83.14 ± 8.37	89.28 ± 4.55	0.001*
SOT4	77.06 ± 10.10	80.30 ± 8.41	0.102
SOT5	57.67 ± 13.02	65.82 ± 8.16	0.001*
SOT6	48.46 ± 11.83	59.42 ± 14.42	0.001*
CS	73.13 ± 9.51	76.20 ± 6.07	0.001*

CS, composite score; SOT1, sensory organization test condition 1; SOT2, sensory organization test condition 2; SOT3, sensory organization test condition 3; SOT4, sensory organization test condition 4; SOT5, sensory organization test condition 5; SOT6, sensory organization test condition 6.
*$P<0.05$ considered statistically significant.

Patients with Child–Pugh class C had significantly weaker performances in SOT2, SOT4, and SOT5 ($P<0.005$), SOT6 and CS ($P<0.001$) compared with Child–Pugh class A. Patients with Child–Pugh class C had significantly weaker performances in SOT2 and SOT4 ($P<0.05$), SOT6 and CS ($P<0.001$), compared with Child–Pugh class B (Table 4). Therefore, deterioration in liver functions was associated with greater impairment in balance.

Patients with abnormal cognitive and psychometric functions results in (NCT and LTT) ($n=17$) had significantly weaker performances compared with those with normal test results ($n=28$) in SOT2, SOT4, and SOT5 ($P<0.05$) and SOT6 and CS ($P<0.005$, Table 5).

On performing correlation analysis, there was a significant inverse correlation between NH_3 levels and all posturography findings as shown in Table 5. There was an inverse correlation between NCT-A and posturography findings in SOT1, SOT4, SOT5, SOT6, and CS as shown in Table 5. Further, there was an inverse correlation between LTT and posturography findings in SOT2, SOT3, SOT6, and CS as shown in Table 5.

Table 3 *t*-Test results of sensory organization test findings between high ammonia (group I) and low ammonia (group II)

	Mean ± SD		
	Group I (n=24)	Group II (n=21)	P value
SOT1	90.54 ± 2.55	92.59 ± 2.68	0.012*
SOT2	85.39 ± 4.67	89.64 ± 3.21	0.001*
SOT3	80.65 ± 6.69	85.99 ± 7.33	0.013*
SOT4	73.61 ± 10.37	80.99 ± 8.40	0.012*
SOT5	53.86 ± 13.94	62.03 ± 10.60	0.034*
SOT6	39.31 ± 9.07	59.17 ± 17.42	0.001*
CS	56.93 ± 9.28	74.90 ± 7.44	0.001*

CS, composite score; SOT1, sensory organization test condition 1; SOT2, sensory organization test condition 2; SOT3, sensory organization test condition 3; SOT4, sensory organization test condition 4; SOT5, sensory organization test condition 5; SOT6, sensory organization test condition 6.
*$P<0.05$ considered statistically significant.

Table 4 Mean ± SD of dynamic posturography according to the Child–Pugh classification of patients

	Mean ± SD		
	Child A (n=20)	Child B (n=11)	Child C (n=14)
SOT1	92.49 ± 2.72^{a}	90.09 ± 2.05^{a,b}	89.19 ± 1.06^{a,c}
SOT2	89.66 ± 3.17^{a}	83.33 ± 3.09^{a,b}	81.92 ± 5.04^{a,c}
SOT3	85.29 ± 8.31^{a}	82.48 ± 5.17^{a,b}	80.59 ± 6.01^{a,c}
SOT4	81.81 ± 8.84^{a}	74.04 ± 11.40^{a,b}	72.61 ± 8.11^{a,c}
SOT5	62.99 ± 11.38^{a}	58.66 ± 10.26^{a,b}	49.28 ± 6.25^{a,c}
SOT6	60.86 ± 10.07^{a}	43.60 ± 10.42^{a,b}	34.94 ± 5.22^{a,c}
CS	75.54 ± 8.14^{a}	68.50 ± 6.62^{a,b}	63.71 ± 9.22^{a,c}

Groups bearing same initials differ statistically at $P<0.05$.
CS, composite score; SOT1, sensory organization test condition 1; SOT2, sensory organization test condition 2; SOT3, sensory organization test condition 3; SOT4, sensory organization test condition 4; SOT5, sensory organization test condition 5; SOT6, sensory organization test condition 6.
a, b and c are indicate whether there is a statistically significant difference between each group and the other or not. Groups having same initials as (a and ab) or (a and ac) have ststatistically significant difference while groups not having same intials as (a and ba) or (a and ca) do not have ststatistically significant difference.

Table 5 Correlation between dynamic posturography results with each of NH_3, NCT-A, and LTT

	NH_3		NCT-A		LTT	
	r	*P* value	*r*	*P* value	*r*	*P* value
SOT1	−0.321	0.031*	−0.326	0.029*	−0.177	0.246
SOT2	−0.522	0.001*	−0.280	0.062	−0.380	0.010*
SOT3	−0.407	0.005*	−0.262	0.083	−0.323	0.030*
SOT4	−0.359	0.015*	−0.368	0.013*	−0.218	0.151
SOT5	−0.547	0.001*	−0.390	0.008*	−0.274	0.068
SOT6	−0.659	0.001*	−0.455	0.002*	−0.329	0.027*
CS	−0.648	0.001*	−0.470	0.001*	−0.371	0.021*

CS, composite score; LTT, line tracing test; NCT-A, number connection test-type A; NH_3, ammonia; SOT1, sensory organization test condition 1; SOT2, sensory organization test condition 2; SOT3, sensory organization test condition 3; SOT4, sensory organization test condition 4; SOT5, sensory organization test condition 5; SOT6, sensory organization test condition 6.
*$P<0.05$ considered statistically significant.

Discussion

Several studies have been carried out on patients with HE to evaluate neurological and neuropsychiatric characteristics [7,10,11]. However, in this study, we objectively quantified balance and postural control in patients with liver cirrhosis and examined the influence of deterioration in liver functions in cirrhotic patients and grade of HE on the balance control of these patients. We found statistically significant weaker performances in the results of SOT tests on comparing the patient and the control group, as shown in Table 2. According to Monsell *et al.* [12], posturography is designed to evaluate postural and balance control while standing. In our study, there were lower scores in psychometric test (NCT-A and LTT) results between the patient and the control group (Table 1). Moreover, when we classified patients according to Child–Pugh scores, we found that Child–Pugh class C patients had the lowest performances in the dynamic posturography tests (Table 4). Therefore, we concluded that the frequency and/or severity of impairment in balance control increases with the progression of liver disease, and progression from Child–Pugh class B to Child–Pugh class C cirrhosis is associated with a marked decrease in postural control. This could possibly be because of the increasing frequency and severity of HE in advanced liver disease, indicating an impairment in postural control during the course of increasing encephalopathy.

Our results are in agreement with those of Schmid *et al.* [6], who studied the influence of liver cirrhosis and the presence of HE on balance. They divided the patients into two groups: those with alcoholic liver cirrhosis and those with nonalcoholic liver cirrhosis. They found impairment in postural control in patients with liver cirrhosis compared with the control groups in both etiologies. In Egypt, alcoholic liver cirrhosis is uncommon, whereas the most common cause of cirrhosis is posthepatitic cirrhosis mostly caused by HCV, which was the most common etiology (87%) in patients with cirrhosis in this study. On evaluating the effect of HE on postural control, patients with high NH_3 had highly significant weaker postural control compared with patients with low NH_3. This was in agreement with the results of Schmid and colleagues, who found significantly lower scores in SOT1, SOT4, SOT5, and CS in patients with high NH_3. Our results were confirmed by the inverse relation between NH_3 levels and all the SOT results as shown in Table 5. This indicates the influence of the presence of encephalopathy detected by a high NH_3 level on postural control. This provides strong support for the involvement of HE in the genesis of impairment of postural control in cirrhotic patients.

Since 1970, NCTs have been included in the diagnosis of HE by Zeegen *et al.* [13] and have been the most frequently used psychometric tests for the assessment of latent HE. Several studies [14–17] have considered NCT as the most sensitive psychometric test for the diagnosis of subclinical HE, because up to 60% of patients with liver cirrhosis had pathological results in the NCT. Our findings are in agreement with those of Karin *et al.* [9], who studied psychometric measures for the assessment of early HE using NCTs and concluded that NCTs may be a sensitive test for the diagnosis of early HE, but they recommended age-related references. In our study, the patient and the control group were age matched to nullify the effect of age on the results of the psychometric tests (Table 1). On comparing the results of psychometric test (NCT-A and LTT) scores between patients and controls, a statistically significant difference was found (Table 1).

As impairment in postural control is one of the manifestations of HE in patients with liver cirrhosis, we found that patients with abnormal results of cognitive and psychometric functions (NCT-A and LTT) showed worse SOT results compared with those with normal test results. Furthermore, there was also a significant inverse correlation between the results of NCT-A test (duration of the test) and SOT in SOT1, SOT4, SOT5, SOT6, and CS, and LTT test and SOT in SOT2, SOT3, SOT6, and CS (Table 5). This was in agreement with the results of Schmid *et al.* [6], who found a significant inverse correlation between the results of NCT-A test and posturography.

Conclusion

HE because of liver cirrhosis affects balance control and the degree of affection is related to the degree of encephalopathy. Dynamic posturography tests could be useful in the investigation of postural control in patients with liver cirrhosis. Therefore, we recommend using dynamic posturography as a possible tool to identify the early effects on balance among patients with liver cirrhosis. However, the size of the study sample was not large enough; hence, further studies with a large sample size should be carried out.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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