

# Diagnosics in Liver Diseases

## 10 Neurological and psychological diagnostics

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## 10 Neurological and psychological diagnostics

► There are **two basic dimensions** in the way the human brain copes with everyday routine; these are known as crystalline and fluid intelligence (R. B. CATTELL, 1963).

1. **Crystalline intelligence** is acquired by education and experience; it proves susceptible to disturbance at a relatively late stage in life and to a relatively small extent. • Crystalline (cognitive and verbal) intelligence implements the contents of what has been learned or acquired at an earlier stage to perform tasks or to solve problems. This verbal (“cognitive”) intelligence is retained for a long time, so that any impairment of cerebral function is noticed at a relatively late stage in people who pursue mental occupations.

2. **Fluid intelligence** depends largely on the speed at which information is processed; it becomes impaired relatively early and to a greater extent. • Fluid (practical and nonverbal) intelligence is characterized by the capability for solving new problems without reference to experience or education in the course of processing information. This form of intelligence deteriorates at an early stage with any impairment of cerebral function, which is why the intelligence involved in performing practical tasks, so-called handling intelligence, is most susceptible to disturbance – it is for this reason that manual activities are primarily impaired.

► Many different **brain functions** are available to enable routine everyday tasks to be mastered correctly. (s. tab. 10.1)

1. Attentiveness
2. Intellectual capacity
3. Logical thinking
4. Memory for design
5. Perceptive faculty
6. Power of concentration
7. Psychomotoricity
8. Reactive capacity
9. Short-term memory
10. Spatial perception and mental comprehension of numbers or letters, *etc.*

**Tab. 10.1:** Brain functions important for mastering routine everyday tasks

### 1 Brain disorders in liver diseases

In cerebral dysfunction, it is possible for disorders to be reflected individually in differing states of intensity and in various combinations. This results in a diverse pathophysiological and clinical picture of **encephalopathy**. Such a collective term for restrictions in the function of the brain does not, however, yield any statement as to their origins or pathogenesis. Encephalopathy can be triggered by some 50–60 disorders and aetiological factors – including liver diseases. (*see chapter 15*)

**Hepatic encephalopathy (HE)** is defined as a functional, potentially reversible disorder of the brain in the wake of severe (either acute or chronic) liver disease. The term comprises all neurological and mental symptoms.

Diagnosis of the four clinical stages of **manifest HE** (stages I–IV) is simple and reliable. But it is important firstly to recognize **latent HE** (stages 0, 0–I), also called *subclinical hepatic encephalopathy (SHE)* or *minimal HE*. • At this stage, no clinically identifiable mental or neurological defects can be detected, nor do the laboratory parameters provide any real clues. Yet, some (still reversible) neurophysiological and neuropsychological deviations from the norm can be quantified.

**Early diagnosis of HE at the latency stage** is significant in social terms, for industrial medicine and for prognostics; therefore it is of enormous economic importance as well. The development of latent (minimal and subclinical) or subsequent manifest HE (stages I–IV) depends on various factors. • *Latent HE is seen as the “most frequent complication” in hepatology.*

### 2 Diagnosis of disorders in cerebral performance

It should be noted that the diagnosis of latent HE (stages 0, 0–I) can cause great **difficulties**.

Despite the considerable medical and social implications of SHE, which in objective terms are undeniable, the patient subjectively feels unchanged and free from symptoms. There are no ailments or malaise felt by the patient which point to the development of SHE, and neither the conversation with the physician nor the anamnesis are suggestive of this condition. *Verbal intelligence is not affected!*

Neither clinical findings nor laboratory parameters (including intensive and scientific tests) correlate with the stage of SHE. There are no neurological abnormalities (no hyperreflexia, tremor or asterixis, etc.). • *For the diagnosis of subclinical hepatic encephalopathy, only electroencephalographic and neuropsychological (psychometric) test procedures are available so far.*

#### 2.1 EEG

**Spontaneous EEG** can occasionally show a minimal increase in slow waves and a deceleration of the basic activity below the normal alpha wave range (8–12 Hz), yet there is no correlation with the oc-

currence of SHE. Only with knowledge of the individual's normal state and with the help of the regular spontaneous EEG as follow-up procedure for cirrhosis can SHE be recognized in 30–50% of cases. However, this is not feasible on a regular basis. With the manifestation of HE (stages I, II), the spontaneous EEG slows down to the theta and delta wave ranges (4.0–7.5 and 1–3 Hz), which are deemed to be pathological in a waking state. Groups of relatively even waves at a rate of two or three times per second, and above all frontotemporal delta Faren rhythms, are considered to be hints of a more severe HE. (7, 18, 20, 29, 43, 44, 47)

**Visually evoked potentials:** In the diagnosis of SHE, neither the use of visually evoked potentials (VEP) nor acoustically or somatically evoked potentials yielded better results than the spontaneous EEG. Using these exogenously evoked potentials, functional disorders of sensory pathways are identified by assessing the P-100 wave. (2, 10, 12, 21, 26–28, 36, 43, 47, 49–51)

**P-300 wave:** The technique of *endogenously evoked potentials (EEP)* can be applied for the registration of stimulus assessment processes and “attention processes”. The *P-300 wave* is deemed to be the electrophysiological correlate of stimulus assessment processes (E. DONCHIN, 1979). P-300 latency indicates the time required for assessment and categorization of a stimulus. About 30% (45) to 71% (16) of patients with SHE and some 70% (45) to >85% (16) of cases with stage I HE show a lengthening in the latency of the P-300 wave. The sensitivity of this test procedure for the diagnosis of SHE is therefore good. The specificity is minimal because of the widely differing origins of HE. • Determination of the P-300 wave is, however, both time-consuming and expensive, calling for specialized knowledge and experience. For this reason, the process is not suitable as a routine test. • *Nevertheless, in diagnosing SHE, assessment of the P-300 wave in an endogenously evoked EEG is seen as the most valuable neurophysiological method of examination.* (5, 11, 26, 37, 42, 48)

► The use of **proton MR spectroscopy**, with glutamine as a marker, has opened up new diagnostic horizons. (35)

## 2.2 Neuropsychological test procedures

In order to objectify disruptions in brain performance, numerous test procedures have been established in clinical psychology. With the help of these procedures, various cerebral functions can be tested. (s. tab. 10.1)

The term **psychometrics** signifies the most objective recording possible concerning mental functions and personality features with the aid of a variety of test procedures.

**Quality criteria and secondary criteria:** Test procedures applied in clinical psychology should fulfil the requisite **quality criteria** including (1.) objectivity, (2.) reliability, and (3.) validity. • Alongside these main criteria, neuropsychological test procedures should also incorporate other **secondary criteria**, such as (1.) standardizability,

(2.) comparability, (3.) cost factor, (4.) usefulness, and (5.) sensitivity. • *Obviously, it will not always be possible to meet all of these criteria in full in every case.*

*No single test is absolutely reliable or even accurate.* The results of neuropsychological tests are subject to various **influences** and thus confounded by a number of factors occurring individually to differing degrees of intensity and in a variety of combinations. (s. tab. 10.2) • This no doubt explains the widely differing assessments of the frequency of SHE which are reported in the literature. An examination of several of the multiple brain functions (s. tab. 10.1) requires the skilful selection of test procedures with their respective targets.

### 1. Influential factor “test procedure”

- desired test targets
- suitable test combination
- professional implementation of the test

### 2. Influential factor “liver disease”

- severity
- aetiology and pathogenesis
- acute or chronic state
- portosystemic collaterals

### 3. Coexistent factors

- consumption of alcohol
- cerebral noxae
- cerebral or cerebrovascular damage

### 4. Individual factors

- age
- intelligence
- social status
- fluctuation in the course of SHE

**Tab. 10.2:** Factors influencing the reliability of test results and the detection of SHE frequency

Quite clearly, it is not a single test, but rather a **combination of tests**, focusing on as many different brain functions as possible, which guarantees an overall result that is meaningful.

**Neuropsychological tests:** Among the large number of neuropsychological tests available, several procedures are considered apt for the detection of subclinical brain disturbances. Some involve complex methods and call for specialized knowledge. Nevertheless, a few can be regarded as the “*gold standard*” for clinical issues involved in the diagnosis of SHE. (1, 6, 15, 17, 43) (s. tab. 10.3)

**Test combinations:** For clinical purposes, suitable test combinations can be set up on the basis of the overview given (s. tab. 10.3) and in accordance with the respective issues. Due to their feasibility and reliability, the following tests are particularly useful: (1.) basic intelligence test, (2.) multiple-choice vocabulary intelligence test, (3.) short test for general intelligence, (4.) short test for cerebral intelligence, (5.) attentiveness-concentration test, (6.) Benton test, (7.) syndrome short test, and (8.) trail-making test. • In clinical studies, the Wechsler adult intelligence scale (WAIS) is often used. (14, 38, 41) In such studies, the WAIS verbal IQ is seen to be largely undisturbed, whereas there are clear deficits in that *part of the WAIS which relates to performing practical tasks* (handling IQ), particularly in the number-symbol test and in the mosaic test. At the same time, other psychological test procedures are applied, mainly the trail-making test as well as EEG (VEP, P-300 wave).

### 3 Basic psychometric programme

► The principle of early diagnosis and early treatment of a disease together with the prevention of a progressive or complicated course are fundamental targets in everyday medical routine. *This applies especially to latent hepatic encephalopathy, which can be found in a high percentage of patients suffering from liver disease.*

#### Intellectual capacity

1. Hamburg-Wechsler adult intelligence test (D. WECHSLER, 1964); 60–90 minutes
2. Basic intelligence test (R. B. CATTELL et al., R. H. WEISS, 1972)
3. Multiple-choice vocabulary intelligence test (S. LEHRL, 1977); 5–8 minutes
4. Short test for general intelligence (S. LEHRL et al.); 8–10 minutes
5. Short test for cerebral intelligence (S. LEHRL et al.)

#### Powers of attention and concentration

6. Attentiveness and concentration test (R. BRICKENKAMP, 1968); 5 minutes
7. Revision test (G. MARSCHNER, 1972); 8 minutes

#### Memory

8. Benton test (A. L. BENTON, 1953)
9. Syndrome short test (H. EERZIGKEIT); 15 minutes
10. Mini-mental-status test (M. L. FOLSTEIN et al., 1975); 10 minutes
11. Wechsler memory test (D. WECHSLER); 45–60 minutes

#### Recognition of shapes

12. Visual-design-potential test (L. BENDER, 1946); 20 minutes

#### Speed of cognitive performance

13. Trail-making test (parts A and B) (R. M. REITAN, 1955)
14. Number-connection test (part A of trail-making test, fourfold variations) (H. O. CONN, 1977)

#### Reactive capacity

15. Measurement by technical appliances
  - speed of response
  - accuracy of response

**Tab. 10.3:** Neuropsychological test procedures with respective test target priorities (and average duration of test)

### 3.1 Psychometric test procedures

Obviously, the EEG examinations and psychological tests outlined above are not suitable for use at the doctor's surgery or in clinical routine as a screening programme for the presence of SHE. Although they meet the required quality criteria, they are time-consuming and cost-intensive, and thus unacceptable. • In the past thirty years, some 50 simple *psychometric screening tests* have been developed and reports made on their appli-

cation (in a variety of combinations). (4, 6, 8–10, 14, 15, 19, 22, 23, 25, 30, 31, 34, 38, 40, 41, 43, 45) (s. tab. 10.4) • The *multiple-choice determination device* is another test which has proved its worth.

1. Alphabetic deletion test
2. Archimedes spiral test
3. Block design test
4. Circle-dotting test
5. Colour word test
6. Digit-span test
7. Dot test
8. Handwriting-specimen test
9. Line-labyrinth test
10. Line-tracing test
11. Logical inductive test
12. Memory for design test
13. Number and symbol test
14. Perceptual maze test
15. Raven's matrices test
16. Serial-subtraction test
17. Star-construction test
18. Story-retelling test
19. Tracing of geometric figures
20. Visual motor design test
21. Visual retention test
22. Word-pair retention test

**Tab. 10.4:** Selection of psychometric screening tests (in alphabetical order)

#### 3.1.1 SIP

Use of a questionnaire comprising 136 questions relating to the "sickness impact profile" (SIP) indicated a marked decrease in patients' capacity to perform routine daily activities and a diminished quality of life in 27% of cases of latent HE. (9)

#### 3.1.2 Mechanical testing procedures

With appliance-based tests, it is possible to measure both reaction time and accuracy of response.

**Multiple choice determination device:** Five electronically controlled coloured light pulses (yellow, red, green, blue, white) are activated in alternating sequences. Pressing a button with the same colour indicates that the test person has recognized and registered the colour both instantly and correctly. This device has proved to be a useful instrument in clinical testing environments. (14)

**Posner test:** This mechanical testing procedure is designed for measuring spatial-visual attention and orientation (M. I. POSNER et al., 1988). The test persons are required to sit in front of a computer monitor using a cross in the middle of the screen as a fixation point. A square is visible on either side of the cross. In the neutral position, a question mark is displayed as a cue 200 milliseconds before the stimulus (= asterisk) appears in one of the squares. In the valid position, the cue is an arrow directed towards the square where the stimulus will appear. In the invalid position, it is directed towards the



opposite square. When the stimulus appears, the test person pushes a button as quickly as possible. The Posner test reveals the varying delay in reaction time in patients with cirrhosis; it does not appear to have a higher sensitivity than the number-connection test. (1)

**Critical flicker frequency:** The principle of flicker-fusion frequency analysis was first introduced by E. SCHAFHÄUTL in 1855 and later developed for clinical use by L. GOLDBERG in 1943. This method has since been widely used in differential diagnosis of organic brain syndromes. • It was first established in patients with latent HE in 2002. (13) The patient observes what appears to be a constant red light shining on the screen, but which is in fact flickering at a high frequency. This flickering is normally detected by the test persons above 42 light pulses/sec with individual variations. However, in patients with latent HE, this occurred below 39 pulses/sec (cutoff value), in HE stage I below 36 pulses/sec, and in stage II below 32 pulses/sec. The results are independent of the patient's education level; there is no learning effect when the test is repeated. (39)

These simple psychometric screening tests do, however, have certain **disadvantages**, which have to be considered when results are being assessed. (s. tab. 10.5)

1. Several complementary screening tests are required for the identification of SHE
2. It has not been adequately defined which functional brain areas are covered by the tests
3. Standardized test evaluation is often not possible
4. There is still no adequate basis for comparison with scientifically established test procedures in neuropsychology

Tab. 10.5: Disadvantages of psychometric testing

### 3.2 Psychometric test programmes

Based on the results in the literature (which also correspond to our own experience), psychometric test programmes have been developed for use in the hospital and the doctor's surgery.

1. Simple to carry out
2. Easy to assess
3. Low time factor
4. Minimal costs
5. Reproducibility
6. Semiquantitative evaluability
7. Allows examination of various functional areas or performance capacity of the brain (even if not specifically defined or differentiated)

Tab. 10.6: Requirements for psychometric test procedures relevant for application in the doctor's surgery

Such test programmes make it possible to objectify neuropsychic disturbances and hence yield semiquantitative identification of the subclinical (latent) stage (0, 0–I) as well as manifestation stage I (or I–II) of HE. These programmes can be considered relatively reliable owing to the standardized instructions for their implementation and adequate objectivity in the evaluation process. A psychometric test programme suitable for use in the doctor's surgery and at the hospital should meet the **requirements** given above. (s. tab. 10.6)

1. **PSE syndrome test** (W. HAMSTER, M. KLICK, H. SCHOMERUS): The **short form of the test** is comprised of (1.) number-connection test (part A) and (2.) line-tracing test. The test results are converted into standard values according to age. • The **long form of the test** is made up of (1.) number-symbol test, (2.) number-connection test (part A), (3.) circle-dotting test, (4.) target-fixing test, and (5.) line-tracing test.

2. **Psychometric test set** (E. KUNTZ, H.-D. KUNTZ): This test set facilitates psychodiagnostic monitoring of potential liver-diseased patients, identification of SHE and control of therapeutic measures. The *four basic tests* can be evaluated in their overall assessment with even greater reliability using *supplementary tests*, which are likewise easy to implement. (19) (s. tab. 10.7)

#### Basic tests

1. Handwriting-specimen test
2. Number-connection test (part A)
3. Line-tracing test
4. Star-construction test

#### Supplementary tests

1. Serial-subtraction test
2. Story-retelling test
3. Mechanical testing procedures

Tab. 10.7: Psychometric test programme for identification and monitoring of SHE (E. KUNTZ, H.-D. KUNTZ, 1991) (19)

#### 3.2.1 Handwriting-specimen test

The handwriting-specimen test (I. SZAM, 1977) is a simple procedure providing insight into fine motor control. Subtle changes in the handwriting are thought to be a sign of constructive apraxia, i. e. there are disturbances in carrying out learned expedient movements, although the powers of perception and mobility are still intact. The possibilities of using *medical graphology* in hepatology have been presented in detail in the literature. (24) • **Regular handwriting tests are quite correctly known as the "poor man's EEG".**

► In line with neurophysiological findings, the patient should write his first and last name and *not* texts, place-names or dates! *The signature constitutes a swift, habitual sequence; as a reflex action which does not involve the application of willpower; it is considered to be a person's graphological identity.* In the early stages of HE, fine, swift and controlled movements of the hand are impaired. The handwriting-specimen test correlates well

with the number-connection test and the subtraction test. • *Impaired handwriting* is reflected in small jagged peaks, hooks, interruptions in the flow, subtle irregularities, fluctuations in pen pressure, size of the lettering, etc. The assessment is based on the subjective criteria of the physician, which is, however, perfectly adequate for hospital or surgery purposes. (s. figs. 10.1; 15.3) • In addition, the results can be graded according to the physician’s personal scoring system. (s. tab. 10.8)

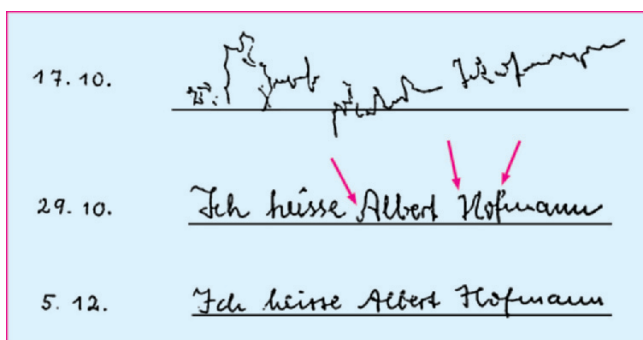


Fig. 10.1: Specimens of a patient’s handwriting (first name and surname) in stage II (17 Oct.), in the SHE stage (29 Oct.) and in a normal state (5 Dec.) (s. fig. 15.2)

Changes	Score (points)	Stage of HE
not detectable	0	no HE, stage 0
very minimal or minimal	1	SHE, 0 – I
moderate	2	I, I – II
clearly evident	3	II
pronounced	4	II – III

Tab. 10.8: Assessment criteria for the handwriting-specimen test

### 3.2.2 Number-connection test

The **trail-making test** (R. M. REITAN, 1955) originated from the “army individual test” (1945) and the test results of S.G. ARMITAG (1946). It comprises two parts: the *number-connection test (NCT)* with numbers from 1–25 (part A) and the *number and letter combination test (NLCT)* with numbers from 1–13 and the letters A–L (part B). (32, 33) (s. fig. 10.2)

The *NCT* presented by H.O. CONN in 1977 (3) corresponds to part A of the *number-connection test* as described above; however, four different test sheets are used, each with a different arrangement of figures. In this way, a possible learning effect from sheet to sheet is ruled out. The four different test sheets are of equal difficulty and generally require the same period of time to complete. • With NCT and NLCT (parts A and B), logical thinking, powers of concentration and perception, together with the capacity to handle three-dimensional numbers and letters are assessed. Swift cognitive speed in thought processing is called for as well as the capacity to adapt. (19, 38, 46, 49)

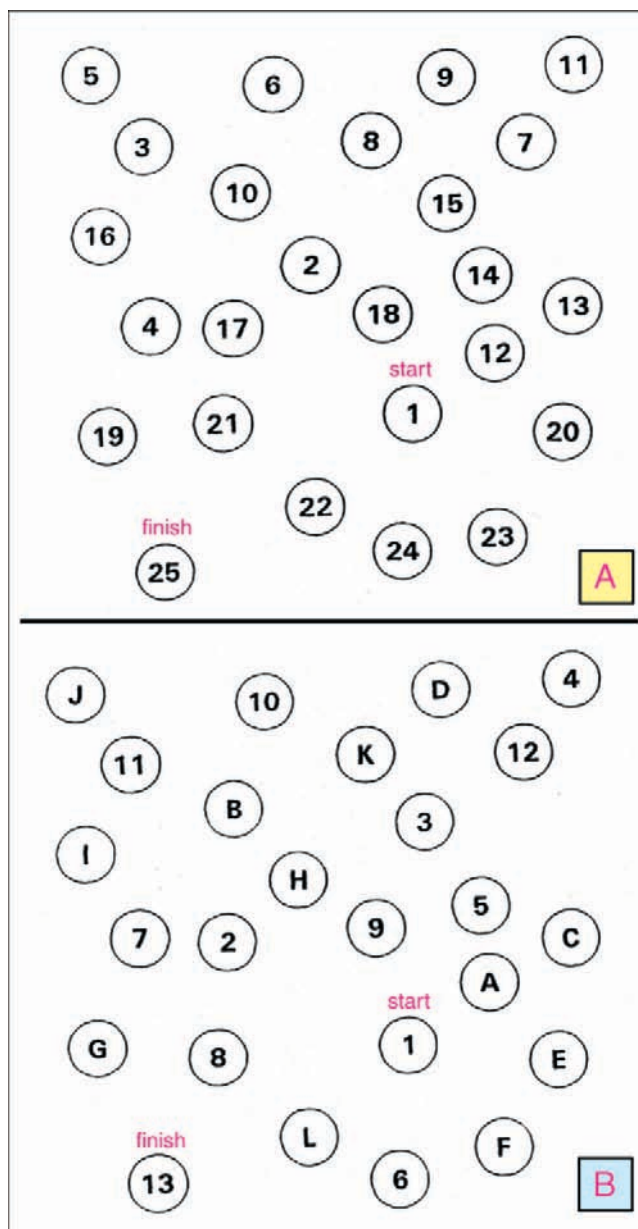


Fig. 10.2: Number-connection test (NCT; part A) and number-letter-connection test (NLCT; part B) (R. M. REITAN, 1955; H.O. CONN, 1977)

Time in seconds	Score (points)	Stage of HE
< 40	0	no HE, stage 0
41–60	1	SHE, 0 – I
61–90	2	I, I – II
91–120	3	II
> 121	4	II – III

Tab. 10.9: Assessment criteria for the number-connection test (NCT; part A)

► In order to complete the test, either the 25 figures in part A or the numbers 1–13 in consecutive alternation with the letters A–L in part B have to be correctly linked up by lines as quickly as possible, whereby any corrections are included in the time allotted.

If the patient is unable to complete the test within 150 seconds, it is broken off. The last correctly linked number and the respective time are noted (e.g. 17/150). The time required by the patients for part A of the number-connection test, as used by us in the psychometric examination set, allows a relatively reliable clinical interpretation to be made. In the number-connection test (part A), the **normal value** should be set at no more than 40 seconds. • The relevant score can be noted as an assessment criterion. (s. tab. 10.9)

### 3.2.3 Line-tracing test

The line-tracing test (LTT) is used to determine the accuracy of a person's fine motor control. A test sheet (s. fig. 10.3) shows a relatively complex "road map", 5 mm in width (corresponding to a 2.5 m wide lane). The patient is asked to trace this not-so-easy path with a pencil from start to finish, as quickly as possible, without going over the edges. The number of errors provides a semiquantitative assessment. • In addition, the respective number of points can be recorded on the score sheet. (s. tab. 10.10)

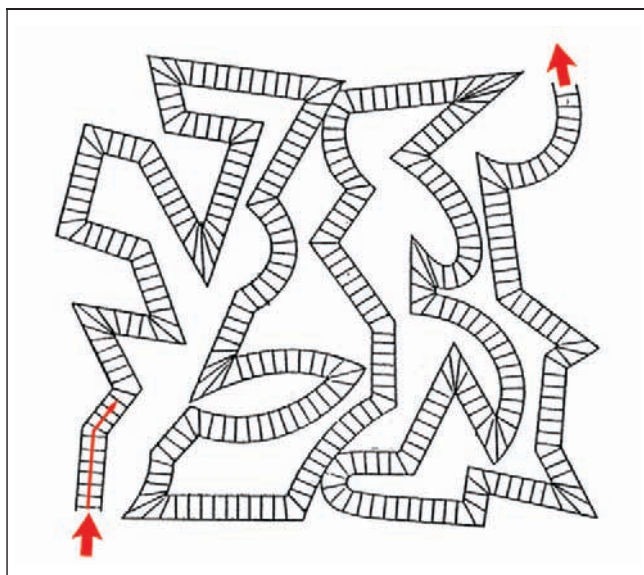


Fig. 10.3: Line-tracing test (LTT) using a difficult path, 5 mm in width (corresponding to a 2.5 m wide lane on a normal road)

### 3.2.4 Star-construction test

The star-construction test examines the patient's psychomotor function, recognition of shapes, and short-term memory. A test sheet (s. fig. 10.4) is presented to the patient, who is requested to look at the five-pointed star drawn on it for about ten seconds (E. A. DAVIDSON et al., 1956). (4) The test sheet is then covered or turned over. The patient is now asked to copy the star using 10 matchsticks, whereby the tips of the matches should form the pointed tips of the star. A lack of precision or errors in arranging the matchsticks and/or any confusion which arises during the test are rated as mistakes. • In addition, the respective number of points can be recorded on the score sheet. (s. tab 10.10)

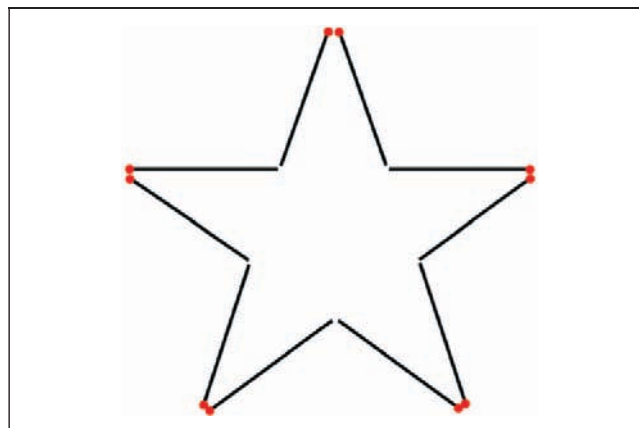


Fig. 10.4: Star-construction test (E. A. DAVIDSON et al., 1956) (4)

Number of errors	Score (points)	Stage of HE
no error	0	no HE, stage 0
0–2	1	SHE, 0 – I
3–5	2	I, I – II
6–9	3	II
> 9	4	II – III

Tab. 10.10: Assessment criteria for the line-tracing test and star-construction test

► The results of these four tests can be summarized by means of their score to give a **total number of points**, thereby simplifying the clinical interpretation in the individual case. (19)

The **time needed** for each test procedure (explanation, implementation and evaluation) is three to four minutes, provided the necessary test materials are already at hand (test sheets, stop-watch, pencil, matchsticks, etc.). • It is possible to have the tests carried out by trained personnel.

These simple test procedures can be executed in any surgery. A code number could be assigned as the *cost-calculation item* for health-insurance purposes. • It is neither organizationally possible, nor medically justifiable, let alone financially viable to make the implementation and assessment of these tests dependent on a specific professional qualification, such as is acquired in further education programmes. • *Every doctor is capable of carrying them out!*

If it is impossible to assess the presence of SHE with these tests, some additional, basic **supplementary tests** can be applied at the surgery. They require no test materials. The time needed for each test is three or four minutes.

### 3.2.5 Serial-subtraction test

With the help of the serial-subtraction test, the patients' powers of attention and concentration can be easily



tested as well as their short-term memory and mental arithmetic capabilities.

From a specific initial figure selected at random (such as 100 or 110 or 130), the patient is asked to deduct another number, likewise selected at random (= subtract), continuing the subtraction procedure through a number of steps by “mental arithmetic” (e.g.  $100 - 7 = ?$ ,  $- 7 = ?$ ,  $- 7 = ?$ ). After the third or fourth arithmetical step, a patient with SHE and a disturbed short-term memory usually no longer knows which number he/she has to deduct from which previous result. This simple test can likewise be adequately quantified for practical purposes. • *If the test is repeated, the same numbers can be taken for the same patient and the results compared. There is virtually no learning effect involved.*

### 3.2.6 Story-retelling test

Another psychometric supplementary test that can be used is the retelling of a story. Here the patient’s short-term memory, perceptive faculties and logical thinking are tested.

The physician tells the patient the following story (lasting about one minute), which then has to be retold by the patient (also in about one minute): *“A bee flies to the brook to take a bath and falls into the water. A dove sees the bee and saves it from drowning. The dove lays the bee on a leaf to dry off. The next day, a hunter comes into the wood and takes aim to shoot at the dove. The bee flies at him and stings the hunter’s hand so that his shot misfires.”* It is important to note any **incorrect renderings of the plot** which are typical of SHE – e.g. the hunter or the dove drown, the dove stings the bee, the hunter shoots the bee, the dove stings the hunter, etc.

## 4 Synopsis

► Such a test programme makes screening for SHE very simple; it is reliable for both surgery and hospital purposes. The test sheets and test results should be documented and filed for an appropriate period of time. • Patients who display cerebral dysfunction during these simple tests generally show more pronounced impairment of cerebral functions when complex and specific test procedures are applied. • *Psychometric tests are highly sensitive as regards disturbances in cerebral performance, yet they have no specificity regarding underlying causes or the disease itself – for this reason they are not “specific to the liver” either.*

► In suspected subclinical hepatic encephalopathy, psychometric tests are extremely important for the diagnosis and cannot be substituted by other examination procedures (e.g. anamnesis, inspection, laboratory analysis, imaging techniques).

► The transition from the latent stage (SHE) to stage I of clinically manifest HE can be gradual, as demon-

strated by the results of the psychometric tests. In this *transitional zone (SHE I)*, there may occasionally be minor neurological findings, such as hyperreflexia, fine tremor or asterixis. (s. p. 272) (s. tab. 15.5)

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