Standardization of the Tübingen flicker test

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Abstract. In the Tübingen flicker test, the subjective brightness of a steady field is adjusted to that of a flickering test field at 50-0 Hz. This test has proven itself as a valuable and highly specific method in the diagnosis of optic neuritis (ON). This paper reports on the development of new judgement criteria and their standardization, based on a new cohort of 527 eyes, 138 of them with florid ON. After improving the conditions of examination and evaluation the optimal criteria for the definition of a pathological result were determined in an explorative manner that is described in detail. The criteria finally chosen are defined such that they preserve the high specificity (98%) of the test, while also retaining a high sensitivity (85.5%).

Introduction

The Tübingen flicker test has proven itself to be a valuable method in diagnosing optic neuritis (ON). This test has been performed in our department on more than 1000 eyes, 250 of them with florid ON. Previously we reported on a first cohort of 527 eyes and found a high specificity and sensitivity of the test [1, 2, 25, 29]. At that time, due to technical limitations, most of the patients could not be examined at low flicker frequencies (<10 Hz) and some atypical cases could not be definitely categorized.

Therefore, a new study, based on a totally new cohort of another 527 eyes, was carried out with the aims:
1. To improve the conditions of examination and evaluation with increased attention given to the results at flicker frequencies between 10 and 0 Hz
2. To define new judgement criteria, which preserve the high specificity of the test and allow a reliable categorization even in atypical and subsiding cases

This paper deals exclusively with the development of the new criteria and their standardization; a report on the clinical results of this study has already been given [26-28].

Patients and methods

The evaluated cohort consists of 279 patients with 527 eyes, 138 of them with florid ON, 52 with subsided ON, 155 normal eyes, and 182 eyes with other diagnoses.

The diagnosis ON was made when at least four of the following symptoms were present: sudden monolateral visual loss, central scotoma, afferent pupil defect, spontaneous remission, normal or swollen optic disc at the onset and partial optic atrophy during follow-up, transient visual blurring due to exercise or exposure to high temperatures (Uhthoff phenomenon), painful movement and/or pain at pressure on the eye, and delayed latencies of the visual evoked potentials (VEPs).

In this paper, the term “ON” refers to cases of primary inflammation of the optic nerve, isolated or in association with multiple sclerosis; it does not include cases due to spread of inflammation from contiguous tissues.

“Florid” ON implies an active inflammation, i.e., the visual functions are subject to change. A “subsided” ON was assumed, when the active stage is completely over, i.e., visual acuity has reached its final level and there is no complaint of an Uhthoff phenomenon.

In the Tübingen flicker test brightness sensation (subjective brightness) of a flickering light is measured. A double projector (Halogen lamp 3000° K) projects two semicircular half-fields onto a screen to form a circle, split by a narrow line. The ray-path of one half-field is interrupted by a rotating sector disc with a light-dark ratio of 1:1, thus causing approximately rectangular flicker stimuli, the frequency of which can be varied between 50 and 0 Hz by the investigator. The luminance of the nonintermittent, steady half-field can be controlled by the patient. The patient has the task to adjust the subjective brightness of the steady field to that of the flickering field.

The optimal main examination parameters, test-field luminance and size, were determined by Honegger [16] and used during the previous study and remained unchanged:
1. Test field size = 7° diameter
2. Test field luminance at steady light = L (0 Hz) = 32 cd/m²

The parameter flicker frequency was extended to the range 10-0 Hz and the measurements were carried out at the following flicker frequencies: 50, 40, 30, 25, 20, 15, 10, 8, 5, 3, 2, 1, and 0 Hz.

Above critical fusion frequency (CFF), i.e., above 40-50 Hz, and with a light-dark ratio of 1:1, the intermittent stimulus is perceived at one-half the brightness of the luminance of the steady field according to Talbot’s law [24]. The time-averaged luminance at 50 Hz flicker is 19.5 cd/m² (= 80 au), rather than the expected 16 cd/m², because of the slight amount of light added to the test.
field by the room illumination. Therefore, the test is performed under photopic luminance conditions with a suprathreshold stimulus.

The test is done monocularly in a moderately dark room (if possible, with corrective glasses), beginning with the healthy or better eye, which is examined from 50 Hz with decreasing frequency to 0 Hz. After that the examination of the 2nd eye is carried out in the same way.

The adjustment scale of the device ranges from 1 to 80 cd/m² (0–99 au). When, as happened infrequently, patients reported an even higher brightness sensation than 99 au, this could not be taken into consideration and was registered as 99 au. The brightness values of the steady field adjusted by the patient are read in au on a digital scale of the device. If necessary, they can be converted into luminance values (cd/m²) in line with the characteristic curve of the apparatus (Fig. 1). Because of the shape of this characteristic curve, the scale of luminance values on the ordinates of Figs. 2–5 is only approximately logarithmic. At the end of the examination, the measured brightness values are graphed onto a printed form revealing pathological values at a glance.

The test does not presume good visual acuity, because it is based on comparing the brightness of large areas of a clearly suprathreshold luminance. However, a visual acuity of at least 0.1 is necessary for obtaining usable results.

The determination of the CFF resulted during the measurement of brightness sensation as additional data, since the examination covers frequencies above and below CFF.

Because of its modest specificity we did not include the CFF results in this paper.

Evaluation procedure

Figure 2 shows schematically the brightness sensation of normal persons (broken line) and of patients with ON (thick solid line). Above CFF (above 40–50 Hz), subjective brightness specifies the Talbot level (line 2, 80 au = 19.5 cd/m²) in normal eyes and ON.

It must be emphasized that in the Tübingen flicker test brightness sensation of a flickering light is determined monocularly in comparison with a steady light. When two test fields of equal brightness are compared binocularly and haploscopically, of course, the affected eye's sensation of both flickering and steady light is darker than that of the healthy fellow eye. That means that in reality, the total curve of brightness sensation, including the Talbot level, is located on a lower level in ON than in normal eyes. This has been shown by Honegger [16] with haploscopic examination as well as by Sadun and Lessell [22] with alternate occlusion. This deficit in brightness sensation of the involved eye, however, is not specific for florid ON [16, 22] and, therefore, was not considered for our graphic representations.

Since the test starts at 50 Hz, the graph is designed such that the curve, reading from left to right, corresponds to the course of the examination.

In normal persons (broken line), brightness sensation increases with decreasing flicker frequency. At 8–10 Hz subjective brightness of the flickering light is enhanced above the brightness of the steady stimulus at 0 Hz, known as the Brücke-Bartley effect (a) [3, 4, 9–11, 20, 21, 31, 33]. Then the curve returns to the luminance at 0 Hz (line 1, 87 au = 32 cd/m²).

In ON, by contrast, brightness sensation decreases to a minimum (b) when flicker frequency is lowered. Then the curve either returns to the luminance at 0 Hz or exhibits a brightness enhancement at 1–3 Hz, which we call "late maximum" (c).

The results were evaluated using two completely independent procedures:

1. Preliminary trial: manual evaluation of all results under double-blind conditions (the flicker test results of each patient were interpreted without knowledge of the other data; the clinical diagnosis was ascertained without knowledge of the flicker test results). Therefore, a priori preliminary