INDUCED PUPILLARY OSCILLATIONS*

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THE ease with which the iris can be observed, combined with the long course of the nervous pathways, accounts, in great measure, for the extensive literature on pupillary reflexes. Much of this work has been undertaken by clinicians seeking guidance in diagnosis. Yet, in most present-day investigations, use is made of complex apparatus which is far from suitable for use in routine clinical examination. It was therefore with some interest that we noted that Stern (1944) had briefly described a simple technique for investigating pupillary activity.

If a slit-lamp is adjusted so that the vertical image of the slit falls on the edge of the iris and just overflows into the eye and on to the retina, the pupil becomes smaller after a short latent period. As a result, the beam of light is partly or completely cut off from the retina, and the pupil then enlarges to near its previous size. The retina, being re-exposed to light by this dilatation, again initiates a reflex contraction of the iris, and the cycle of events is repeated. In this way it is possible to set up sustained, and easily observed, oscillations of the iris. As a result of these oscillations the retina receives a series of light stimuli whose frequency and duration is dictated by the behaviour of the iris. The frequency and duration of the oscillations depend on: (1) the latent period of contraction of the iris; (2) the duration of the contraction; (3) the latent period of dilatation of the iris; (4) the duration of the dilatation. The frequency of the oscillations is such that the latent period of contraction must encroach on the dilatation phase, and the latent period of dilatation must encroach on the contraction phase.

Loewenstein and Friedman (1942), and Loewenstein and Schoenberg (1944), using pupillography in the examination of early unilateral glaucoma and neuro-syphilis, observed, in consecutive pupillary contractions, a prolongation of one or more of the above periods in all except in the first few successive contractions of a series. Such a change, if it is sustained, should be interpreted also, and more simply, as a change in the frequency of induced pupillary oscillations. As a preliminary to a clinical investigation it was therefore decided to assess the reliability of the technique on normal subjects under the various conditions likely to be met in clinical work.

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Apparatus and Method

The observations were carried out in a dark room: we used a Gullstrand clinical slit-lamp, which, to stabilize the conditions under which the experiments were performed, was fed from a constant voltage transformer, and the light output checked from time to time with a photometer. The slit of the slit-lamp was at maximum aperture. The pupil margin was observed by means of a biomicroscope with low-power objectives. A chin- and forehead-rest steadied the subject's head, and fixation movements were greatly reduced by placing before the subject's right eye a small adjustable mirror, in which he could fixate the reflection of the faintly glowing filament of a 12-volt car-lamp about five metres away. The oscillations were timed by means of two stop-watches calibrated in fifths of a second.

The subject was comfortably seated, and the mirror before his right eye adjusted to make the fixation point appear to be directly in front. In each of the experiments the slit-lamp was placed so that the angle of incidence of the light on the subject's eye was 30° to 45° to the temporal side of the optical axis of the left eye. The image of the slit was brought to a focus on the iris. The pupil margin was then observed through the binocular microscope, and the light brought to the edge of the iris until it just entered the pupil. As soon as a regular oscillation had become established, one stop-watch was started during the contraction phase of a cycle, and ten complete oscillations were timed. The watch was then handed to a clerk who recorded the reading to the nearest fifth of a second, while the observer continued his observations with a second stop-watch. Ten groups of ten contractions were usually timed in continuous series. From time to time during a period of observation there were involuntary eye movements. In such cases timing was stopped, and only resumed when the "hippus" was re-established. It was found most suitable to measure the time taken for ten complete oscillations. This time was converted into frequency of contraction per minute.

In many instances a 16 mm. cinematograph film was made of the oscillations by means of ultra-violet light and panchromatic film. This allowed direct measurements to be made on the amplitude and frequency of the iris movements.

Results

Position of the slit of light on the iris.—After some trials at inducing this pupillary oscillation it was noticed that the position of the slit of light on the iris appeared to influence the frequency and amplitude of the oscillations. In order to estimate the effect of the position of the light, readings were taken with the light alternately

just at the pupil margin and then further towards the centre of the pupil.

With the slit of light placed centrally, the oscillations were irregular in frequency and amplitude, and consequently difficult to count. With the light just overlapping on to the pupil, however, the frequency was regular, of good amplitude, and well sustained. In the subsequent experiments, care was taken to have the light at the pupil margin.

Fatigue.—Fatigue of the light reflex has been demonstrated by Lowenstein and Friedman (1942). They found that, with a recurrent light stimulus of one second duration every three seconds, the iris excursion began to diminish after the fifth stimulus, the effect developing gradually until, after the sixtieth stimulus, there was almost complete immobility of the iris. The light response of this immobile iris could be restored by a psychosensory stimulus such as a sudden sound, or the suggestion of fear or pain. Among the changes in the pupillogram ascribed to fatigue were diminished amplitude of contraction and dilatation of the iris, and prolongation of the latent period of contraction up to 0.4 second. Fatigue of such rapid onset would be expected to show in our observations, where 100 oscillations usually followed in a continuous series. We found no falling-off in frequency, such as might have been expected if the latent period of contraction had been prolonged to 0.4 second from the normal one of 0.2 second. There was no obvious decrease in the amplitude of the oscillations.

To make assurance doubly sure, a special series of observations was made on both experienced and inexperienced subjects. Here silence was observed, and up to 200 continuous oscillations were directly scrutinized. Again, fatigue was not manifested.

Effect of Preliminary Dark Adaptation.—For the purpose of the experiment a sufficient degree of dark adaptation was obtained by seating the subject (N.A.) in almost complete darkness for a period of thirty minutes. At the end of this period the subject was placed at the slit-lamp, and observation was begun. On receipt of a visual signal, made automatically every thirty seconds, the observer began timing ten oscillations. In the short interval after the timing of these ten contractions, during which the next signal was awaited, the beam of light was directed away from the subject's eye.

Fig. 1 shows the results of two of these experiments performed under identical conditions. It will be seen that during the first five minutes the rate fell from about 85 to a steady mean of 73 oscillations per minute. After dark adaptation the beam of the slit-lamp brought about marked miosis. This miosis wore off in several minutes as light adaptation proceeded.

Effect of Preliminary Light Adaptation.—A sufficient degree of light saturation was obtained by seating the subject (N.A.) with the forehead against an opal X-ray viewing screen for a period of 10 minutes. The screen was illuminated from behind by a 250-watt lamp. Immediately this period of light adaptation had been completed, observations were begun and recorded as described above.

In this series, at the beginning of each observation, the pupil was wider than normal, the amplitude of the oscillations was

FIG. 1.—Effect of light adaptation on the frequency of induced hippus. Time in minutes after a preliminary period of 30 minutes dark adaptation.

smaller, and some difficulty was encountered in inducing the oscillations. Presumably because of these factors, the readings obtained showed a greater scatter about the mean as compared with those illustrated in Fig. 1. The means of three such experiments are shown in Fig. 2. During the first five minutes the rate increased from 60 to 70 oscillations per minute; it remained at this level until the end of the observations.

It will be noted that in the two previous experiments there is no indication that pupillary fatigue is affecting the rate of induced oscillations, even after fifteen minutes' observation.

Effect of Altering Light Intensity from the Slit-lamp.—To investigate the effect of changes in light intensity on the frequency of the pupillary oscillations, a means was required of effecting rapid and predetermined changes in the light intensity of the slit-lamp beam. A delay in effecting this change might have allowed retinal adaptation to modify the results obtained. We therefore introduced into the low-voltage supply to the lamp, a variable resistance which was connected to a two-way foot-switch. The resistances were adjusted so that in one position of the switch the lamp was being overloaded by 20 per cent. of its rated voltage, and in the other

FIG. 2. Effect of relative dark adaptation on the frequency of induced hippus. Time in minutes after a preliminary period of ten minutes light adaptation.

position the lamp was being under-run to such an extent that the intensity of the light was just sufficient to induce pupillary contractions. As measured by a barrier-layer photo-electric cell, the light intensity in the second position was 6 per cent. of that in the first. This range of experimental conditions far exceeds that likely to occur as a result of mains voltage fluctuation during clinical work.

The subject (T.W.) was dark-adapted for a period of 5 minutes. A series of twenty readings, each of ten oscillations, was then made, during which the light intensity was alternately high and low. In this way the effect of any retinal adaptation that might occur fell equally on each group. The results obtained during low-intensity illumination had a mean of 61.5 oscillations per minute as compared with the mean of 70.1 oscillations per minute during high-intensity illumination. The "t" test applied to these

results showed a significant difference in the means at the 1 per cent. level of significance.

Correlation of Pupil-Size and Frequency of "Hippus."—From the previous experiments we had formed the impression that the frequency of the oscillations induced was higher when the pupil was small than when it was large. The relationship of frequency of

FIG. 3. Correlation between the frequency of induced hippus and simultaneously noted pupil size in one subject.

oscillation to pupil-size was therefore investigated. A graticule eyepiece was used to make an estimate of pupil-size while ten oscillations were being timed. This approximation in the measurement was inevitable, as one figure had to represent the mean pupil-size during the ten oscillations counted. It was decided to make the measurement at the maximum period of dilatation while the pupil was in hippus. The graticule scale was read to the nearest quarter of a division, 0.16 mm. of actual pupil-size. In Fig. 3 the

mean frequency during each group of ten oscillations is plotted against the estimated mean pupil-size. For the fifty observations made, the correlation ratio of 0.309 is significant; that is, an increase in pupil-diameter is associated with a decrease in the frequency of the oscillations.

Inaccuracies inherent in this method may account for the results which lie outside the general trend. Further investigations are being made with the help of cinematography.

The Effect of Exercise.—There was a possibility that the differences observed in the experiments on light and on dark adaptation might be due in part to the fact that during dark adaptation

FIG. 4. Frequency of induced hippus after five short periods of exercise. The mean results of two experiments are presented.

the subject had been physically at rest for a period of 30 minutes, whereas, during light adaptation, the period of rest was only of 10 minutes. As an indication of the extent to which this initial resting period might be responsible for changes in the rate of the oscillations, the effect of exercise was investigated.

The exercise consisted of stepping up and down from a chair six times. As an initial trial showed that the effect was apparently transient, the exercise was repeated at stated intervals during the course of the experiment. In order to allow the subject to settle down, and to eliminate the effect of previous retinal adaptation, readings were made every 30 seconds for five minutes before exercising, a steady mean thus being reached after two or three minutes. The mean results of two experiments are shown in Fig. 4. Moderate exercise produced a rapid drop in the frequency of the oscillations. Soon after the exercise stopped, the frequency

began to return to its normal level at rest and reached it in about 10 minutes.

Examination of a group of normal subjects.—Thirty men and thirty women were examined under constant conditions. The total number was confined to sixty as, in the available subjects, the range in ages was not sufficiently wide to permit an accurate examination of a possible correlation between oscillation frequency and age. In this experiment, the age of the majority of the subjects was between 19 and 25 years with extremes at 17 and 36 years. These subjects—mostly medical students—were healthy, and with no complaint apart from a refractive error of moderate degree in a few cases.

The iris colour was noted, and, in addition, in 37 subjects the pulse-rate was taken immediately before and immediately after observing the pupil, the mean pulse-rate being noted. No significant difference was found in the frequencies observed in men and

FIG. 5. Correlation between the frequency of pupil oscillation and of resting pulse in 38 subjects.

in women. In the complete group, the mean frequency was 68.9 oscillations per minute and the standard deviation was 11.3 oscillations per minute. In the 37 subjects whose pulse-rate was also noted, a positive correlation was found between this rate and the oscillation-frequency of the pupil (Fig. 5). This data gave a positive correlation ratio of 0.408 which is significant at the 1 per cent. level.

The frequency of pupillary oscillations thus appears to be positively correlated with the heart-frequency in a group of subjects. From experiment on exercise, however, we know that in a person subjected to moderate exercise the rate of oscillation decreases, whereas the pulse-rate increases. It seems therefore that, if such a correlation exists in the individual, it is readily broken down by any external stimulus, such as exercise, which causes pupil-dilatation and increase in heart-frequency.

One subject was examined on several occasions over a period of four days, pulse-rate and pupil-oscillations rate being noted simultaneously. In the 45 readings which were taken, no significant correlation was established between frequency of pulse and pupil-oscillation.

In the group investigated there was no correlation between oscillation-frequency and age or colour of the iris.

Discussion

The frequency of the pupillary oscillation induced under our relatively simple standard conditions seems to exhibit a high degree of uniformity in normal subjects belonging to the rather restricted age-group, 17-36 years. Such uniformity in normal subjects should make deviation from the normal easily detected in disease.

The results of the experiment in which pupil-size is compared with the frequency of oscillation, indicate the association of a smaller pupil with a higher frequency of oscillation. This observation may explain the results obtained after light-adaptation, dark-adaptation, change in intensity of the slit-lamp, and exercise. In these experiments the factor which is associated with fewer contractions per minute is also associated with a pupillary constriction. Pupil size seems to be the dominant factor. We can hazard no more than a guess as to the cause of this effect. It may be that the iris, when the pupil is small, is in a physical state to respond more rapidly to changes of illumination of the retina. This association of pupil size and frequency of contraction is being examined in greater detail by means of cine-photography in a further investigation.

The absence of fatigue is striking and in direct contradiction

to the findings of Loewenstein and Friedman (1942). The discrepancy may be due to differences in technique.

It should be noted that the iris can contract more rapidly than it does under the conditions of the present work. Bartley (1942) found that the iris could respond to short-duration stimuli, individual contractions of the iris being obtained for frequencies of up to 180 stimuli per minute. At higher frequencies no oscillation occurred.

Summary

1. When the beam of a slit-lamp falls on the iris and overlaps on to the pupil to reach the retina, a sustained series of iris oscillations takes place.

2. For reliable results it is necessary to adjust the slit so that the beam just encroaches on the pupillary margin. If the beam falls near the centre of the pupil the rhythm of the contractions becomes irregular.

3. Previous dark-adaptation of the retina causes an increase in the rate of these oscillations during the first five minutes of adaptation to light stimulation.

4. Previous light-adaptation causes a decrease in the rate of the oscillations during the first five minutes.

5. Sudden and marked changes in the light intensity of the slit-lamp affect the pupillary rate. An increase in the intensity causes an increase in the oscillation rate; a decrease in the intensity causes a decrease in the oscillation rate.

6. Exercise of the subject shortly before beginning the test causes a decrease in the rate of oscillation, possibly as a result of pupil dilatation.

7. A significant negative correlation is found between pupil-size and frequency of oscillation. It is suggested that the effects of light- and dark-adaptation, light intensity, and exercise may be explained on the grounds of their effect on pupil size.

8. Age, sex, and colour of iris do not significantly affect the frequency of pupillary oscillations.

9. A significant positive correlation is found between resting pulse-rate and frequency of pupillary oscillations in a group of normal subjects.

10. Pupillary fatigue does not significantly affect the frequency or amplitude of the oscillations.

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