PUPILLARY REACTIONS TO SINGLE LIGHT PULSES IN PSYCHIATRIC PATIENTS AND NORMALS

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Psychiatric patients and normal controls were compared for pupillary responsivity, under dark-adapted conditions, using single pulses of light presented via a Ganzfeld. Data were collected with electronic equipment, and averaging techniques were used in the analysis of continuous response curves. Results showed that recently admitted patients tend to have slightly smaller pupillary diameters than normals, when at rest, and exhibit substantially attenuated reactivity to light stimulation. Consideration is given to possible artifacts, and findings are interpreted in terms of the known physiological characteristics of pupillary innervation.

Substantial literature has been accumulating, wherein pupillary motility is found to relate to a variety of specific physiological variables (4, 12, 14). In terms of pupillary responses to discrete light and other stimuli, and with respect to variations in reactivity associated with organic and functional disorders, there is much evidence to support the study of pupillary mechanisms as functions of autonomic balance, neural activity, and information processing.

The anatomic pathways of the pupillary light reflex (12, 18) consist of both sympathetic and parasympathetic representations. Fibers from the retina bifurcate before the lateral geniculate, then synapse in the pregeniculate nucleus, and proceed via the pretectal area and Sylvian aqueduct to the Westphal-Edinger nucleus in the third nerve nucleus on both hemispheres. Approximately 50 per cent decussation occurs.

The Westphal-Edinger nucleus sends out efferent fibers via the ciliary ganglion to the sphincter muscle of the iris. The parasympathetic component is opposed by two dilatory mechanisms. One is the excitation of the radial iris muscles, via the cervical sympathetic chain, originating in the vegetative centers of the midbrain. The other is an inhibitory mechanism which acts on the Westphal-Edinger nucleus, receiving its neural activity from several centers, such as the posterior hypothalamus, reticular formation, areas four and eight, and frontal cortex.

While the dilation effected by the activation of the iris dilator muscle is rather rapid, the dilation due to the inhibition of the Westphal-Edinger nucleus is relatively slow. Study of the temporal characteristics of the response permits differentiation between the two. A number of the relationships between pupillary motility and localization of specific lesions in the central nervous system, in both afferent and efferent pathways, have been dealt with by Lowenstein and Lowenfeld (13, 14).

Reliable correlations with organic disturbances have prompted investigators to search for similar relations between pupillary responses and mental illness. In fact, at the turn of this century, such relation-

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ships were suspected by several psychiatrists. Summaries of the pertinent literature by Bumke (2) and Bach (1) are examples. The major problem with these early reports was their contradictory nature. Bumke claimed that dilation of the patient’s pupil, in response to a painful stimulus, signified a favorable prognosis, while absence of the dilation indicated a poor prognosis. Oswald (17), another German psychiatrist, claimed the opposite.

In 1907, Westphal (22) described a specific form of responsivity, which he called the “catatonic pupil,” because of its high incidence in catatonic patients. Lowenstein and Westphal (15) described four types of response to light stimuli, one of which was most common among psychiatric patients; this was characterized by sluggish contraction to light onset, and slow redilation following stimulus cessation. Abnormal reactions in psychiatric patients, to stimulation by light and nonvisual stimuli, have also been reported by Levine and Schilder (10) and May (16). More recently, some seven patterns of adrenergic-cholinergic imbalance, at rest and under stress, have been described by Rubin (19, 20), on the basis of pupillary reactions to light and darkness. Compared with the reactions of normals, patients tended to react either excessively or insufficiently, or both, to appropriate stimulation.

A previous report from this laboratory (7) attempted to distinguish between the pupillary reactions of acute and chronic patients and normal controls, using cycles of 1-second light and 3-seconds darkness. Acute patients were found to have smaller initial diameters than did either the chronic patients or the controls. The pupillary reaction to light showed only that patients tended to reach maximum contraction in less time than did normals. The present report is based on data obtained with more precise and sophisticated methods of recording and analysis.

PROCEDURE

SUBJECTS

Fifty-one recently admitted patients, at the Brooklyn State Hospital, and 31 normal volunteers served as subjects. All subjects were free of neurological and ophthalmological pathology and received no psychoactive medication for at least 10 days prior to testing. The median age of patients and normals was 30 and 22 years, respectively, with the range for both groups being 18 to 45 years, the period during which the effect of age on pupillary reactivity is minimal. Twenty-one of the patients and 15 of the normals were females. According to preliminary examinations by the hospital staff, most of the patients were diagnosed as schizophrenic—paranoid and mixed or undifferentiated types. Seven were described as psychopathic personalities, with or without complications of drug addiction or chronic alcoholism. All patients were tested within 30 days of hospitalization.

METHOD

Each subject was seated in a ventilated dark booth, and dark-adapted for 10 minutes. A headrest device with a biteboard permitted the subject to maintain a fixed position relative to the apparatus, during stimulation and measurement, and to move out of that position between trials. While the subject fixated a dim red spot, located “at infinity,” with his right eye, the eye was scanned and pupil diameter was recorded. Measurements were obtained with an infrared scanning device, developed by Lowenstein and Lowenfeld (General Precision, Pleasantville, N.Y.), which measures the pupil diameter electronically 60 times/second. The diameter is converted into a proportional voltage, which in turn is stored on magnetic tape. Averaging procedures were used, thereby increasing the reliability and precision of the records beyond levels of spontaneous oscillation. The equipment has been described elsewhere (6).
The stimulus, a 30-msec light of 0.3-mL luminance, was presented to the subject's left eye via a Ganzfeld. A brief tone signaled the subject to position himself, and 3 to 5 seconds later the stimulus was presented. A random delay was used to minimize any possible conditioning effects. Three seconds after light onset another tone informed the subject that the trial was over and that he could relax. After a 30-second intertrial interval, the procedure was repeated, for a total of 10 trials/subject.

Both stimulus intensity and pupillary responses were monitored on a two-channel oscilloscope (Tektronix, Inc., Beaverton, Ore.). A calibration pulse was inserted into the response curve of each trial, and subsequently was averaged with all the responses, a method which served to determine the absolute diameter of the pupil and as a check upon the accuracy of the averaging procedure. Recorded response curves were fed into the computer of average transients (CAT), and the normalized curves were plotted with a Moseley X-Y plotter.

RESULTS

Data were analyzed in terms of initial diameter at the moment of light onset, extent of contraction, and the speeds of contraction and redilation. The latter measures were obtained from the first derivatives of the contraction curves, which were computed simultaneously with the diameter records. Mann-Whitney U tests and rank order correlations were used for comparisons between the groups.

Initial diameter scores showed that the patients tended to have smaller pupils than did the normal controls. The median diameter for patients was 6.4 mm; for normals it was 6.9 mm. The difference is significant at the .01 level. There was, however, considerable overlap between the groups on this measure, and predictability of the individual response was low. This tended to confirm previously reported observations for acute patients and normals.

Much more striking, and in contrast to former findings, were the observations of the extent of the pupil contractions to light. The median patient contraction was 1.40 mm, while for the controls it was 1.79 mm, a difference significant beyond the .001 level of confidence. These data are presented in Figure 1 in the form of a cumulative distribution, where the ordinate represents the per cent of subjects in each group whose contraction exceeded a given value on the abscissa. Thus, by empirically selecting 1.70 mm as a cut-off line, it was seen that a contraction of 1.70 mm or less comprised 86 per cent of the patient sample, whereas a contraction greater than 1.70 mm represented over 80 per cent of the normals. From these data it is predictable that a given normal will be correctly assigned to the normal group 80 per cent of the time, and a given patient correctly assigned 86 per cent of the time, on the basis of pupillary responses to light. Male-female differences, and differences attributable to age, revealed no statistical differences. The rank order correlation between age and extent of contraction for all subjects combined was .27; for patients alone it was .037, and for normals only it was .077.

Since the distinctive amplitudes of contraction might be erroneously interpreted as a function of differences in initial diameter

Fig. 1. Cumulative distributions of patients and normals as a function of the extent of contraction to a single light pulse.
—that is, the larger the initial diameter, the larger the scope for contraction—a subsample of 21 subjects was selected from each of the patient and normal groups to yield matched pairs in terms of initial diameter. Thus the median initial diameter was the same for both groups. The data for this subsample, again in the form of a cumulative percentage plot, are virtually identical to the total groups shown in the previous figure. Figure 2 shows the difference between the matched normal and patient groups, which confirms the findings of the difference between psychotics and normals, even when the effect of initial diameter is ruled out. The consistency of these results in conjunction with those obtained from a small group of chronic patients, i.e., smallest extent of contraction and sluggish redilation, relative to normals (11), would seem to be a reflection of some underlying physiological mechanism.

Latency and speed characteristics of the pupillary reaction were analyzed only for 19 normals and 42 of the recently admitted patients, since these data were derived from a first derivative circuit and calibration procedure installed after a number of the original subjects had been tested.

Thus, the maximum speed of contraction was significantly greater for normals than for patients. This measure yielded a rank order correlation coefficient of .78 with the extent of contraction. Contraction latency did not, however, discriminate between patients and normals.

Redilation latency (the time required for the pupil to complete the contraction to light, return to the initial diameter level, and begin to dilate in response to darkness) showed substantially longer latencies for normals than for patients. This finding is essentially a function of the relative shapes of the contraction curves for the patients and normals.

Another measure of pupillary recovery, the maximum speed of redilation (MSR) appeared to be faster in patients with larg-
chiatric patients (3). Since some of the present patients received phenothiazines until as little as 10 days prior to being tested, it is possible that slight ocular deposits had occurred, and consequently less light reached the patient's retina—thereby reducing the amplitude of the contraction to light. This melanosis argument is, however, opposed by several factors. Five patients, who showed minimal contraction responses, were examined by an ophthalmologist with the slit-lamp, and no opacities were found. Also, the long term dosage of 300 mg or more of phenothiazines, administered daily, on which the melanosis reports were based, was rarely attained in our recent admissions. Finally, the results obtained by Granger (5), showing differences in visual threshold between patients and normals of about 0.5 log units, would tend to support the clinical distinctions in the present findings. Granger's data were obtained in the early 1950's, predating the extensive use of pharmacotherapy.

From other studies in this laboratory, on the effects of light intensity on the pupillary contraction response, it has been inferred that the 39-mm median difference in extent of contraction between patients and normals is of the order of a stimulus intensity difference of 1 log unit with normal subjects.

Another artifact, which has yet to be completely excluded, is related to the tendency for phenothiazines to lodge in the tissue of the retina to a greater extent than in other brain structures. Small effects could thereby reduce the efficiency of the light-processing characteristics of the neural elements in the retina, so that the current results might be generated by drug effects, rather than by a characteristic of psychiatric disorder.

In any event, the empirical findings have established that: 1) There is a smaller initial diameter in the patient group. While this is a small effect, it has been found reliably in two studies. 2) There is less contraction of the pupil to light in patients. This is a large effect, which, while prominent only in the present study, dramatically differentiates patient from normals.

On the basis of the pupil's neural pathways, it may be said that finding 1, above, is consistent with the interpretation of reduced sympathetic activity (smaller initial diameter). Finding 2, above, is consistent with either increased sympathetic activity (contradicting the first statement), or reduced parasympathetic reactivity to light in the patient sample, or the operation of one or the other artifacts referred to. The interpretation of reduced sympathetic activity is not supported by the results of the sample which was matched for initial diameters; in fact, those data are consistent with either reduced parasympathetic or increased sympathetic reactivity.

The relevance of arousal level to these patient-normal discriminations is emphasized, as a result of findings by Lowenfeld with normal subjects under the influence of amphetamines. Although amphetamines are presumed to raise arousal level, Lowenfeld observed that initial diameter was not affected by the drugs, but that extent of contraction to light was in fact substantially reduced. This raises the possibility that, under certain conditions, the central and peripheral sympathetic activities can become uncoupled.

Evidence from other laboratories favors an underlying process of heightened sympathetic tonus and reactivity in schizophrenia. Venables (21), for example, has found that certain subgroups of schizophrenics manifested higher skin conductance levels than did normal controls. Similarly, Zahn, Rosenthal and Lawlor (23) obtained elevated heart rate and electrodermal orienting responses in chronic schizophrenics. Most recently Kornetsky and Eliasson (9) have reported data with animals, on a simple at-

*Geigy Pharmaceuticals. Personal communication to G. H., 1965.

*Lowenfeld, I. Personal communication, 1966.
tention task, which they interpreted as support for a model of overarousal in certain schizophrenics. The present pupillary contraction results would be in agreement with the higher arousal level in patients than in normals.

In conclusion, then, some rather striking and consistent differences have been demonstrated, in the pupillary reactions to light, between psychiatric patients and normal controls. That these differences may be the results of long lasting side effects of pharmacotherapy appears unlikely, although such doubts have not been completely dispelled. To untangle the components of contraction and dilation of the pupil, studies with other sensory stimuli are in progress, using sound that acts directly on the arousal centers and produces pupillary dilation, and phosphene stimulation to circumvent the optical apparatus in the production of contraction responses.

REFERENCES


