PUPILLARY ABNORMALITIES IN SCHIZOPHRENIA AND DURING MUSCULAR EFFORT.

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THE pupils of a normal subject are generally described as equal, reacting by constriction or dilatation to various stimuli. Inequality of the pupils as an isolated finding is said to be relatively common, but impairment of the light reflex, especially in conjunction with pupillary inequality, is held to be strongly indicative, if not pathognomonic, of organic disease of the nervous system. An exception is the "tonic pupil," for whose abnormally protracted reactions to light and accommodation an organic lesion has not yet been demonstrated. However, impairment of the light reflex is known to occur in subjects in whom there is no evidence of organic nervous disorder. These abnormalities of the light reflex have attracted little attention in this country, and are ignored almost entirely in text-books of neurology and psychiatry. Redlich (1908) made the important observation that muscular exertion might lead to dilatation of the pupil with impairment of the light reflex. Levine and Schilder (1942), in an extensive investigation of this phenomenon, concluded that muscular effort would produce dilatation and impairment of the light reflex in any pupil which initially retained its response to light, and would accentuate a pre-existing abnormality or bring out a latent tendency to impairment of the light reflex. Westphal (1907) first described the pupillary abnormality in catatonic schizophrenia to which the term "catatonic pupil" has been applied. This abnormality consists of pupillary dilatation with impairment of the light reflex, and is usually bilateral. The reactivity to light may vary from moment to moment, or from day to day; or pupillary rigidity may persist for a considerable time, with transient periods of brisk reactivity. Estimates of the frequency of the "catatonic pupil" vary remarkably—from 54 per cent. (Schilder and Parker, 1931) to 3·4 per cent. (Reichmann, 1913). Apparently a higher incidence has been found where repeated examinations have been carried out on the same subjects, but proper comparison is impossible, as the technique of examination has not been detailed by any of the authors.

PRESENT INVESTIGATION.

343 male schizophrenics and 100 mentally normal males, all under the age of 55, were examined for pupillary inequality, after which a constant technique of examination was used to study the pupillary reactions to pain, light and muscular effort.

Technique of Examination.

Examination for pupillary inequality.—This was carried out in subdued light, at the shaded end of a room, with no direct light near the subject, and no "glare" from windows, walls or objects within the room. In practice this amounts to the minimum light intensity in which the pupil of a brown-eyed subject can be studied satisfactorily. Inequality was recorded as being present only if clear-cut.

The light reflex.—This was tested in subdued light, and in the dark when necessary, by suddenly switching on a 2·5 volt pocket flash-light held approximately 1·5 cm. in front of, and 1·5 cm. lateral to, the centre of the pupil, this being just medial to the outer canthus. With the flashlight in this position, and the subject looking straight ahead at a distant object, the effect of accommodation-convergence is eliminated, and any failure in co-operation can be detected easily. If co-operation was inadequate, the light was switched on with the beam directed away from the eye, and then suddenly directed at the pupil. The reaction of each pupil was tested at least three times on each occasion. Subjects were tested twice on separate days for inequality, and impairment of the light reflex; where abnormalities were found, the tests were repeated frequently during the following month.

The response to pain.—This was tested once in subdued light. A piece of surgical lint was placed over the side of the neck (this prevents the fingers from slipping) and a small fold of skin about two inches vertically below the mastoid process was pinched up through the material between the thumb and first two fingers; a firm, steady pinch was maintained for about two seconds, first on one side, and then on the other. If no dilatation at all was observed on testing and re-testing the result was recorded as negative, but the slightest dilatation was recorded as positive. Non-co-operative subjects were excluded.

The response to muscular effort and its effect on the light reflex.—These were studied once, in two stages, in subdued light.

(1) Mild exertion: The subject squeezes two fingers of an assistant as hard as possible with his right hand.

(2) Moderate exertion: The subject flexes his arm against strong resistance by an assistant.

Non-co-operative subjects were excluded.

Table I.—*Composition of Test Group.*

Schizophrenia (all types)		343
Simple	28	
Hebephrenic	82	
Catatonic	18	
Paranoid	98	
Paraphrenia	10	
Schizophrenic dementia	93	
Superimposed on congenital mental defect	14	

Cases of chronic schizophrenia characterized by apathy, a tendency to negativism, occasional hallucinosis and infrequent incoherent speech have been classified as schizophrenic dementia.

Findings.

The percentage figures in the tables are worked out to two figures.

TABLE II.—*Incidence of Pupillary Inequality.*

Diagnosis.	Inequality (total incidence).		Inequality + abnormal light reflex.		Variable inequality alone.		Variable inequality + abnormal light reflex.		Constant inequality (alone).	
	No.	%.	No.	%.	No.	%.	No.	%.	No.	%.
Schizophrenia (343 subjects)	44	13	14	4·1	2	0·59	2	0·59	26	7·6
Controls (100 subjects)	20	20	1	1	—	—	—	—	19	19

Pupillary inequality is much more common in normal subjects than is generally recognized; the difference in incidence between the two groups is misleading, as approximately 30 per cent. of schizophrenic subjects did not co-operate fully. Only glaring abnormalities can be detected if the eyes are continually shifting around or partially concealed by frequent blinking, so it is highly probable that cases of mild inequality were not detected in non-co-operative subjects. The findings confirm the statement of Levine and Schilder (1942) that the "catatonic pupil" is characterized by variation in degree of inequality, as well as by variation in the reaction to light. Thus:

1. Although minor fluctuations in the degree of inequality were found in both groups, they were more common in schizophrenics.

2. Gross variation in the degree of pupillary inequality (i.e sometimes one pupil would be larger; sometimes the other) without abnormality of the light reflex was found in two schizophrenics.

3. Gross variations in pupillary inequality from day to day, with variable impairment of the light reflex, were found in two other schizophrenics.

Abnormalities of the Light Reflex.

It is generally recognized, although seldom taught, that in some subjects the response to successive flashes of light may vary, being poor one moment and good the next. This variation in response occurs more frequently in schizophrenics (10 per cent.) than in normal subjects (3 per cent.), and is often found in schizophrenics whose pupils show consistent impairment of the light reflex on other occasions. The impairment of the light reflex may be closely related to the "startle reaction." A sudden flash of light produces a definite "startle reaction," and it is frequently found that there is little contraction of the pupil in response to the first flash of light, but a brisk response to the second or third.

In resistive and unco-operative subjects considerable difficulty is encountered in judging the reaction to light, as the size of the pupil is continually changing, due to accommodation-convergence on different fixation points, and the effects of forceful deviation of the eyes. As many of these subjects roll the eyes up during examination, a study was made of the effects of strong upward gaze in 100 normal subjects.

Effect of strong upward gaze on the pupil:

*No effect	73
Pupil dilates	5
Pupil contracts	8
Size of pupil unchanged, light reflex sluggish	3
Pupil contracts, light reflex sluggish	4
,, ,, ,, ,, absent	7

It is clear that in resistive and unco-operative subjects an abnormal response to light may be of no pathological significance. Abnormalities of the light reflex, other than those described above, are shown in Tables III, IV and V.

TABLE III.—*Distribution of Abnormalities of the Light Reflex.*

Diagnosis.	Abnormal (total incidence).		Abnormal + inequality.		Abnormal alone.	
	No.	%	No.	%	No.	%
Schizophrenia (343 subjects)	53	15	14	4·1	39	11
Controls (100 subjects)	1	1	1	1	—	—

TABLE IV.—*Incidence of Abnormality of the Light Reflex in Different Mental Disorders.*

Diagnosis.	Number of cases.	Number abnormal.	% abnormal.
Simple schizophrenia	28	4	14
Hebephrenic schizophrenia	82	14	17
Catatonic schizophrenia	18	2	17
Paranoid schizophrenia	98	9	9·2
Paraphrenia	10	2	20
Schizophrenic dementia	93	18	19
Schizophrenia superimposed on mental defect	14	4	24
Congenital mental defect	15	2	13
Controls	100	1	1

TABLE V.—*Analysis of Abnormalities of the Light Reflex.*

Type of abnormality.	Schizophrenia.		Controls.	
	No.	%	No.	%
Sluggish in subdued light only	44	13	1	1
Sluggish in subdued light and in the dark	1	0·29	—	—
Absent in subdued light, sluggish in the dark	5	1·5	—	—
Absent in subdued light and in the dark	3	0·87	—	—

* In many of these subjects the pupil constricted slightly at first, and then returned to its original size.

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In drawing up the above tables the abnormality recorded for each case is the greatest abnormality observed in that subject. In only two cases was the abnormality constant during the period of observation.

The following abbreviations are used in case-histories :

L., left pupil ; R., right pupil ; >, greater than ; =, pupils equal ; fix., light reflex absent ; sl., light reflex sluggish.

The results of examinations on different days are separated by a colon, e.g. result of first examination : of the 2nd : of the 3rd : etc.

Patient W. D—, aged 52, paranoid schizophrenic. Abnormality probably a minor variant of the tonic pupil. Reaction sluggish in subdued light ; adequate, but slower than normal, in the dark. Accommodation-convergence slow (about 5 seconds), and sustained. Tendon reflexes brisk.

Patient H. S—, aged 48, schizophrenic dementia. Fix. L.>fix. R. in light and dark. Accommodation-convergence fair. Tendon reflexes brisk.

In the other subjects the degree ot abnormality varied from day to day, and was often asymmetrical.

Patient N. D—, aged 45, hebephrenic. Variable inequality and variable light reflex. R. sl.>L. : L.>R. sl. : R. sl. = L. sl. : L.>R. : R. sl.>L. sl. : L.>R. : R. sl.>L. sl. : L.>R. : R.>L. : R.>L. : R. = L.

In one patient variation during even shorter periods was observed.

Patient S. L—, aged 36, schizophrenia superimposed on congenital mental defect. 9.20 a.m., sl. L.>R. ; 9.22 a.m., sl. L.>R. ; 9.26 a.m., L.>R. ; 9.30 a.m., L.>R. ; 9.34 a.m., fix. L.>R. sl. ; 9.45 a.m., L. = R. ; 9.47 a.m., L. = R.

Syphilis could be excluded as a cause of the abnormalities in all except two cases ; it is improbable that neuro-syphilis existed in either of these.

TABLE VI.—*Pupillary Response to Pain.*

Diagnosis.	Number co-operating.	Positive %	Negative. %
Schizophrenia	211	66	34
Controls	100	83	17

These figures show diminished sensitivity of the pain reflex in schizophrenics.

Pupillary Reactions to Muscular Effort.

Results are recorded as follows :

— No change.
+ Dilatation.
++ Dilatation + sluggish light reflex.
+++ Dilatation + absent light reflex.

TABLE VII.—*Response to Mild Effort.*

Diagnosis.	Number co-operating.	−%.	+%.	++%.	+++%.
Schizophrenia	212	61	36	2·1	0·52
Controls	100	26	73	1	—

TABLE VIII.—*Response to Moderate Effort.*

Diagnosis.	Number co-operating.	−%.	+%.	++%.	+++%.
Schizophrenia	220	37	45	12	5·5
Controls	100	14	59	27	—

In the schizophrenic group a greater proportion showed no response to muscular effort. In a certain proportion the light reflex was lost altogether, this presumably being due to the bringing out of a latent abnormality. The results in normal subjects are consistent with previous observations that the dilatation and impairment of the light reflex are proportional to the degree of muscular effort (Schilder and Parker, 1931; Levine and Schilder, 1942), but only if the subject is completely relaxed before the test, and the command to carry out the muscular effort is given suddenly. If the subject is told, "I want you to squeeze hard when I count three. Quite relaxed please—one, two, three," the pupil can be seen to dilate on the command "one," and in favourable subjects it dilates by numbers to a maximum on the command "three." In many cases the dilatation on the command "three" is small compared with the initial dilatation. The initial dilatation is accompanied by a subjective sensation of "getting set," but the actual muscular tension developed is small in proportion to the pupillary dilatation.

The Pupillary Changes during Electro-convulsive Therapy (E.C.T.) and Insulin Coma Therapy.

Further study showed that muscular effort is accompanied by dilatation of the pupil and impairment of the light reflex, whatever the state of consciousness. Thus during insulin coma, dilatation of the pupil with diminution of the light reflex occurs always in association with some sort of motor activity, whatever the degree of consciousness—in sopor in association with motor restlessness and resistiveness, in coma with flexor and extensor spasms. This association is particularly noticeable during termination of a coma with intravenous dextrose, the onset of the pupillary changes coinciding with the sudden violent outburst of straining and restlessness that often occurs as consciousness returns. Similar changes occur during motor restlessness in the stage of nitrogen inhalation therapy before loss of consciousness (Levine and Schilder, 1942), and in the motor excitement that occasionally follows E.C.T. Dilatation of the pupil with loss of the light reflex also occurs during the tonic phase of the fit produced during E.C.T.; the pupil remains in this condition during the clonic phase, and returns to normal 5 to 60 seconds after the fit ceases. (In one case the light reflex returned towards the end of the clonic phase.) A "sub-convulsive" dose produces a short muscular spasm with dilatation of the pupil and impairment of the light reflex for a few seconds. The pupil then returns to normal. If a delayed fit occurs, the pupil may return to normal and then suddenly dilate and become fixed to light as the tonic phase comes on. These pupillary changes probably occur during all major epileptic fits, as they were also noted during a fit which occurred spontaneously in a patient

in insulin coma whilst I was actually studying his pupils. The resemblance to the " Redlich phenomenon " is striking—during a fit great muscular tension is accompanied by dilatation of the pupil with loss of the light reflex. The main difference between this and the changes during normal muscular effort lies in the state of consciousness of the subject, and in the degree of muscular tension developed. The pupillary changes during E.C.T. may be considered to be those of severe muscular effort in an unconscious subject.

Discussion.

The Etiology of the Pupillary Changes during Muscular Effort.

Previous discussion on this subject has been concerned with the question as to whether the changes are due to " psychic " causes, or to some special effect of the muscular tension itself. The most recent contribution is that of Levine and Schilder (1942). They concluded that muscular effort produces its effect by inhibition of the pupillo-constrictor centre, and that this inhibition is reflex, due to stimulation of the splanchnic nerves by the rise in intra-abdominal pressure accompanying the muscular effort.

Discussion as to the relative importance of psychic factors and muscular tension has the unfortunate effect of obscuring the two fundamental issues:

1. Are the effects due to nerve impulses directly from higher levels, or are they reflex, due to the muscular tension itself? (The effects occur without any latent period, and so cannot be due to adrenaline or metabolites released into the bloodstream.)

2. If the former alternative is correct, are the impulses from higher levels of psychic or of somatic origin, and what are the underlying physiological mechanisms?

There is considerable evidence that muscular tension *per se* is not responsible for the pupillary changes. It has been mentioned above that the pupillary changes during E.C.T. may be considered to be those of severe muscular effort in an unconscious subject. A study was made of the pupillary changes in patients undergoing E.C.T., modified by the intravenous administration of curare in dosage sufficient to abolish all muscular contraction, except for almost imperceptible movements in the diaphragm and facial muscles. In these patients the pupillary changes were exactly the same as those during unmodified E.C.T. (curare alone had no effect on pupillary size or reaction to light). In other words, motor impulses from " higher centres " can cause pupillary changes in the absence of muscular tension. Also, as stated above, in conscious subjects pupillary changes may precede the actual muscular effort. It is clear that the hypothesis that the pupillary effects are due to raised intra-abdominal pressure is inadequate. The facts indicate that the pupillary changes during muscular effort are due to motor impulses from higher levels.

These impulses may be either psychic or somatic, or both, e.g. psychic factors predominate in producing the pupillary changes—

(1) Whilst " getting set " for voluntary effort.

(2) During the muscular tension associated with emotional stress.

Somatic factors predominate in producing the changes:

(1) During major epileptic fits.
(2) During flexor and extensor spasms in insulin coma.

Any suggestion as to the physiological mechanisms involved is purely speculative. It is usually stated that sympathetic stimulation causes dilatation of the pupil, without any effect on the light reflex. This is manifestly incorrect, as an active dilatation of the pupil must interfere with simultaneous contraction and so cause impairment of the light reflex. There is every reason to believe that the law of reciprocal innervation applies to the movements of the pupil, and that the pupillary effects are due to sympathetic stimulation in combination with simultaneous para-sympathetic inhibition. It is possible that simultaneous sympathetic stimulation and para-sympathetic inhibition are brought about as part of a generalized discharge from the hypothalamic autonomic centres. Thus a rise in blood-pressure, tachycardia, and pupillary dilatation occur during E.C.T. modified by curare, where the changes cannot be due to muscular tension. This autonomic discharge may be initiated by impulses from both cortical and infra-cortical levels, as pupillary changes accompany muscular spasms during the stages of insulin coma where cortical function is abolished (e.g. during flexor and extensor spasms).

Pupillary Abnormalities in Schizophrenia.

In schizophrenia there is a high incidence of diminished pupillary response to pain, light and muscular effort. Hyporeactivity to various other stimuli has been demonstrated in schizophrenics—to thyroid extract, insulin, dinitrophenol, vestibular stimulation and inhalation of hot moist oxygen (Mayer-Gross and Moore, 1944). From the psychobiological standpoint these findings may be correlated with the schizophrenic's lack of normal emotional response to the outside world. It is interesting to note that the term "withdrawal" has been applied to the psychological and physiological changes in schizophrenia (Mayer-Gross and Moore, 1944).

The abnormalities of the light reflex are of particular importance, as they may lead to confusion in the differential diagnosis of schizophrenia from neurosyphilis, and also in the diagnosis of neurological disorders appearing incidentally in known schizophrenics. The term "catatonic pupil," although appropriate, is misleading, as abnormalities occur in mental disorders other than catatonia. I have seen inconstant diminution of the light reflex in mental defectives, and in a subject suffering from simple depression, and it has also been described after epidemic encephalitis (Westphal, 1907), in psychoneurosis, alcoholic delirium, arteriosclerotic psychosis and neurosyphilis (Levine and Schilder, 1942). Moreover, abnormalities are just as common in other types of schizophrenia as in catatonia.

The cause of the pupillary changes is as uncertain as the cause of schizophrenia itself. Schilder and Parker (1931) advance a theory of multiple causation, postulating constitutional, toxic-organic, and psychic factors. There is no doubt that somatic factors, whether constitutional or acquired, play a

part in the production of the pupillary abnormalities, but not everyone will agree with Schilder and Parker in their emphasis of somatic constitutional factors. There is considerable evidence that emotional changes are important in the production of the pupillary abnormalities. In cases quoted by other authors, the relationship of the abnormality to emotional factors is clear-cut; for example, in Westphal's (1907) case of traumatic neurosis, which developed changes whenever the question of withdrawing compensation was raised, and in Levine and Schilder's (1942) patients immediately before nitrogen inhalation and metrazol convulsion therapy. The high incidence of abnormalities in schizophrenics may be correlated with their apprehension, suspicion and timidity, and with the severity of their emotional disturbance. In the present series a considerable proportion of the patients, whose pupils reacted poorly to light, showed gross manifestations of emotional disturbance during examination, and it has been pointed out above that variable impairment of the light reflex may be related to the "startle reaction." Schilder and Parker (1931) attributed the disproportionately high incidence of abnormalities in negro schizophrenics to somatic constitutional factors. It is equally plausible that the high incidence is attributable to emotional factors, as superstition, apprehension and resistiveness appear more commonly in the negro.

It may appear contradictory to stress emotional factors as the cause of the pupillary changes, and at the same time to correlate diminished reactivity to light with "withdrawal." However, "withdrawal" does not necessarily mean apathy—the world of unreality may be actively defended against outside interference. Interfering stimuli may be dealt with by ignoring them, but if a situation such as physical examination interferes with the world of unreality, it creates an emotional disturbance, and is resented and resisted. Thus the apprehension, suspicion, and resistiveness of the schizophrenic are directly related to withdrawal from reality.

There is a close connection between the Redlich phenomenon and the pupillary changes in mental disorders, inasmuch as psychic factors play a prominent part in both, and mental disorders are frequently accompanied by changes in muscular tension. It is possible that the same nervous pathways are involved in both cases. The following case is an excellent demonstration of the close relationship between emotion, muscular tension and pupillary abnormalities.

Patient K. G—, aged 26, paranoid schizophrenic. Actively hallucinated, aggressive, persecuted and pre-occupied with somatopsychic delusions. Routine examination—pupils normal, react well, dilate with muscular effort. He was taken out of the hospital by his relatives, and subsequently had to be brought back; when seen immediately after his return he was quiet—pupils normal. During conversation he developed hysterical tremors of the arms and legs, his comment being, "I need treatment—I've got to get out of here." These tremors could be brought on or terminated by suggestion, so that repeated study could be made of the pupillary changes during "attacks," the changes appearing to be proportional to the extent of the hysterical manifestations. With mild tremors of both arms there was no change in the pupils; with moderate tremors of arms and legs there was slight impairment of the reaction to light; and when severe movements were continually shaking the entire body there was marked impairment of the light reaction. The next day the pupillary reactions were normal.

Summary.

Abnormalities of the pupillary light reflex occur in schizophrenia, and are closely related to the pupillary changes during muscular effort, which are attributed to simultaneous sympathetic stimulation and para-sympathetic inhibition by motor impulses originating in the hypothalamus. Psychic factors are important in the production of the pupillary changes in mental disorders and during muscular effort, but these changes are not exclusively of psychic origin.

From a psychobiological point of view the abnormalities of the pupillary response to light, pain and muscular effort in schizophrenics can be correlated with their hyporeactivity to various other stimuli, and with their lack of normal physical and emotional response to the outside world.

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