Pupillographic Characteristics of Simulated Relative Afferent Pupillary Defects

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Relative afferent pupillary defects were simulated in normal individuals by performing the alternating light test while dimming the light in front of one eye with neutral density filters. Pupillary responses were elicited using a binocular photostimulator and recorded using a binocular television pupillometer. In five subjects, four spatial variables of the pupillary response—contraction amplitude, minimum size, final size, and redilatation amplitude—were measured and compared. Contraction amplitude was found to be the best indicator of small pupil defects. In eight other subjects, the change in contraction amplitude elicited by using filters from 0.3 to 3.0 log units in density was plotted. Amplitude of consensual responses increased as direct responses decreased, and initial constrictions were visible in many subjects at the 1.8 log unit level. The best method for detecting relative afferent pupillary defects using the alternating light test is to compare contraction amplitudes, looking for consensual responses that are greater than direct responses. Invest Ophthalmol Vis Sci 30:1127-1131, 1989

The alternating light test of Levatin1 is a standard clinical technique for diagnosing optic nerve and retinal disorders. The patient is asked to look at a distant fixation target, and a light is alternately shone in each eye while the pupils are observed. The normal pupillary response is a small initial constriction followed by an equivalent redilatation each time the light is moved from one eye to the other.2 An abnormal response is a decrease in size of the initial constriction on one side with redilatation to a larger pupillary diameter when compared to the other side.2 Such an abnormal pupillary response is called a relative afferent pupillary defect. Because of individual variabilities in pupillary response, bilateral (absolute) afferent pupillary defects cannot be diagnosed at the present time.

Relative afferent pupillary defects can be quantified by repeating the alternating light test while placing neutral density filters over the better eye.4 The density of pupil defect corresponds to the density of filter required to balance pupillary responses. Photographic neutral density filters are generally used, with successive steps of 0.3 log units. Because of concerns about retinal adaptation behind the filter, the recommendation has been to stimulate both eyes without the filter between measurements, and to make a decision about pupillary responses within the first few alternations of the light during each measurement.

Simple observation of pupillary responses provides semiquantitative information that is clinically useful, but most questions about pupillary dynamics can only be answered by pupillographic recordings. Although clinicians have been looking at pupils for years, no one has shown what component of the pupillary response is most useful for detecting small afferent pupillary defects. Amplitude of initial constriction, minimum size, amount of redilatation, and final size after redilatation are all measures than could be used. Each of these can be observed clinically, but noting all four simultaneously is quite difficult.

In order to clarify the dynamics of afferent pupillary defects, I recorded pupillary responses during the alternating light test in normals with pupil defects simulated by dimming the stimulus light in front of one eye. Previous investigators have shown the validity of this technique; pupillary reactions caused by optic nerve disease resemble those caused by decreasing the luminance of the stimulus light.5,6

Materials and Methods

Pupillary stimulation and recording were done with a binocular television pupillometer and photostimulator (Applied Science Laboratories, Waltham, MA). Measurements of pupillary diameter to the nearest 0.05 mm were made from a chart recorder tracing. The light stimuli consisted of two tungsten arcs that were independently focused on each eye.
pupil. The source for each eye was directed through a mechanical shutter operated by a programmable controller so that square-wave stimulation of each pupil was attained. An infrared cutoff filter was inserted in front of each light source. The visual angle subtended by each light was 1 degree 27 minutes, and the intensity was $1 \times 10^3$ ft-L. Each light was positioned in the visual field on the horizontal meridian, 6 degrees 20 minutes temporal to fixation. To simulate clinical conditions, I used a non-Maxwellian stimulus: the light beam measured 10 mm in diameter at the pupil and was positioned so that the entire pupil was always inside the projected beam. Fixation was controlled by having the subject view a single 20/40 Snellen letter projected at 18 feet. The room was otherwise dark; background illumination was 0.05 ft-candles.

Two different sequences of photostimulation were used: (1) alternate stimulation of each eye for three seconds (0.16 Hz), simulating the alternating light test at slower rates of alternation; and (2) alternate stimulation for one second (0.5 Hz), simulating the alternating light test at faster rates of alternation. The light stimulus for each eye began when the stimulus for the other eye ceased, with no delay between successive stimuli. Photographic neutral density filters were placed in front of the stimulus light to simulate relative afferent pupillary defects. The filters used varied in strength from 0.3 to 1.2 log units; densities up to 3.0 log units were obtained by combining filters. Each filter was in place for six to eight (3-sec alternation rate) or eight to ten (1-sec alternation rate) cycles of alternation; a series of three to five unfiltered stimuli were then presented to each eye before the next filter was inserted. Responses that were marred by blink or recording artefacts were rejected before data analysis.

The first experiment consisted of stimulation at the two alternation rates, first using no filter, then using a 0.3 log unit filter over either eye, then using a 0.6 log unit filter over either eye. The amplitude of initial constriction, minimum size, final size after redilation, and amplitude of redilation were measured for each response (Fig. 1). Comparisons were then made between direct and consensual responses of the filtered eye.

The second experiment consisted of stimulation at the 3-sec alternation rate, first with no filter, then with 0.3, 0.6, 1.2, 1.8, 2.4 and 3.0 log unit filter densities in order. In other words, filters were presented in sequence beginning with the least dense and progressing to the most dense. As noted above, each series of filtered stimuli was alternated with unfiltered stimuli in order to maintain photopic adaptation. In order to assess the effects of retinal adaptation, the responses to these unfiltered stimuli were measured as well. Each eye was stimulated at a given filter density before going on to the next filter, and neither eye received a filtered stimulus twice in succession (filters alternated from eye to eye). The amplitude of initial constriction was measured for direct and consensual responses of the filtered eye.

Participants in this study included seven women and six men, ranging from 19 to 41 years old. Five subjects were tested in the first experiment and eight in the second. In the first experiment, four subjects were studied at both alternation rates; one subject was studied at the 0.5 Hz rate only. Written consent was obtained from each subject after the nature of the experiments had been fully explained.

Data were analyzed using the Statview 512+™ (Culver City, CA) and Statview II™ (Berkeley, CA) programs on an Apple Macintosh™ (Cupertino, CA) computer.

**Results**

Contraction anisocoria was present in 13 of the 14 subjects. Because of this finding, direct and consensual responses were always calculated from the recording of the filtered eye.

**Experiment 1**

Multiple regression analysis was used to assess the data. The 1-sec and 3-sec results were analyzed separately. The dependent variable was "type of stimulation" (direct or consensual), and each analysis in-
cluded “eye being assessed” and “experimental subject” as independent variables. The initial analysis on the two data sets included “filter density” as another variable; further analyses were done on the 0.3 and 0.6 filter subsets individually, for a total of six data sets. One of the variables of interest—“constriction amplitude,” “minimum size,” “final diameter,” or “redilatation amplitude”—was then included, and the regression was performed.

In every analysis, the equation that included constriction amplitude had the lowest residual sum of squares and the highest F-statistic, with $P < 0.01$ in all cases. Two equations that included redilatation amplitude were statistically significant: one on the pooled 3-sec data, the other on the 0.6 filter subset of that data. No other regressions generated significant F-statistics. Simple linear regression using constriction amplitude as the only independent variable was statistically significant ($P < 0.001$) in all six data sets.

Figures 2 through 5 show the average differences between direct and consensual responses from the 3-sec alternation data.

**Experiment 2**

As filter density increased, the constriction amplitudes of direct responses decreased and those of consensual responses increased in all subjects. Figures 6

![Constriction Amplitudes 0.16 Hz](image1)

![Final Diameters 0.16 Hz](image2)

![Minimum Sizes 0.16 Hz](image3)

![Re-dilatation Amplitudes 0.16 Hz](image4)
Subject 8, Left Eye

![Graph](image)

**Table 1. Average constriction amplitudes**

<table>
<thead>
<tr>
<th>Filter density (log units)</th>
<th>Direct response (mm)</th>
<th>Consensual response (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.64–1.18</td>
<td>0.50–1.17</td>
</tr>
<tr>
<td>0.3</td>
<td>0.56–1.26</td>
<td>0.61–1.20</td>
</tr>
<tr>
<td>0.6</td>
<td>0.34–0.94</td>
<td>0.66–1.44</td>
</tr>
<tr>
<td>1.2</td>
<td>0.18–0.70</td>
<td>0.83–1.60</td>
</tr>
<tr>
<td>1.8</td>
<td>0.07–0.43</td>
<td>0.83–1.83</td>
</tr>
<tr>
<td>2.4</td>
<td>0–0.26</td>
<td>0.98–1.73</td>
</tr>
<tr>
<td>3.0</td>
<td>0–0.09</td>
<td>1.18–2.01</td>
</tr>
</tbody>
</table>

*Range of average constriction amplitudes of direct response and consensual response of the filtered eye at each filter density.*

Fig. 6. Direct (hollow squares) and consensual (dark squares) constriction amplitudes of the left eye of Subject 8 during the alternating light test as filters of increasing density are placed over the eye. Each point represents the average of several responses.

Fig. 7. Direct and consensual responses of the right eye of Subject 11. The smaller consensual responses with no filter in place are a manifestation of contraction anisocoria.

and 7 illustrate the results from one eye of two different subjects. Table 1 lists the range of direct and consensual responses of the filtered eye at each density. A factorial analysis of variance was done at each filter density using the following categories: subject, type of stimulation (direct or consensual), and eye. Direct and consensual responses were significantly different ($P < 0.001$) in all cases, with direct responses being smaller with a filter in place and larger with no filter.

Stimulation with a filter in place tended to create a small relative afferent pupillary defect in the unfiltered eye at higher filter densities. Direct responses of this eye were less than consensual responses during the first few stimulus alternations after testing with filters of 1.2 log unit density and higher, but analysis of variance showed statistical significance at the 1.8 and 2.4 log unit levels only. Comparison with the data previously obtained using filters of lower density showed that the induced relative afferent pupillary defect was in the range of 0.3 log units at the 1.8 level and slightly more after using the 2.4 log filter.

Table 2 shows the cumulative total of subjects with initial constrictions 0.2 mm and 0.3 mm or greater at each filter density; for example, with the 1.8 filter contraction amplitudes measured 0.2 mm or greater in four subjects and 0.3 mm or greater in three of these four.

### Discussion

In an experiment similar to the present one, Sugawara et al. found that both latency of pupil response and maximum constriction velocity varied with density of induced relative afferent pupillary defect; maximum constriction velocity varied linearly with density of filter applied, suggesting that this measure would be the best to use for diagnosing and quantifying pupil defects. However, latencies and velocities cannot be determined without special equipment; I chose to study variables that could be estimated by the clinician.

Retinal adaptation can cause problems when filters are used to simulate relative afferent pupillary defects. When a dimmer light is used to stimulate one eye, that eye becomes more sensitive to light. When equal stimulation is restored, the opposite eye will appear to have a small relative afferent pupillary defect. In this experiment, retinal adaptation had no measurable effect on pupillary responses until filters of density greater than 1.2 log units were used. The sequence of stimulus presentations used here meant that retinal adaptation caused the effect of the filter to be slightly exaggerated at the start and diminished by the end of each series of alternations.

In the current study, a decrease in amplitude of initial constriction proved to be the best indicator of...
low-density, simulated relative afferent pupillary defect. In patients with unilateral or asymmetric optic neuropathies, differences in constriction amplitudes of the two pupils are usually easy to see with a reasonably bright, hand-held light. Occasionally the initial constriction cannot be seen in either eye; when this happens the room should be made as dark as possible, the light should be held on each eye for a longer period of time, or, if necessary, a brighter light should be used.

With the intensity of light used in this experiment, the direct response during the alternating light test decreased while the consensual response increased as denser filters were applied. A similar observation was made by Sun et al.9 With increasing filter density, the pupils tend to be larger when light first enters the consensual eye, because of a decrease in contraction amplitude and an increase in amplitude of redilation of the previous direct response. Intermittent stimulation of the unfiltered eye keeps the mean pupillary diameter in a range where an increase in consensual response amplitudes is still possible, even after the constriction amplitude of the direct response becomes negligible. Pupils that are very large react less well to light than do midsize pupils.10 If the stimulus light had been too dim, the increase in consensual response amplitudes is still possible, even after the constriction during the alternating light test becomes negligible. Pupils that are very large react less well to light than do midsize pupils.10

Some previous descriptions of the alternating light test have indicated that a relative afferent pupillary defect is present when the initial constriction is lost on one side (see, for example, Gittinger11 or Burde et al12). Using this criterion, all pupil defects in Experiment 2 measuring 1.2 log units or less would have been missed, assuming that an initial constriction of 0.2 mm would be visible clinically.

The term, "contraction anisocoria," refers to a pupillary response that is greater in the stimulated eye than the opposite eye. This difference in response amplitudes is most noticeable when the stimulus comes from the temporal visual field, as in this study. Because of contraction anisocoria, relative afferent pupillary defects can only be diagnosed when the consensual response of one pupil is larger than its direct response. The only alternative would be to compare direct responses of the two pupils, but asymmetric direct responses are caused more often by simple anisocoria than disease.

To detect a relative afferent pupillary defect, the clinician should look for a difference in amplitude of initial constriction of the two pupils during the alternating light test, and a pupil defect should be diagnosed when the consensual response is greater than the direct response.3 Clinical papers that mention relative afferent pupillary defects should state what criteria and techniques were used to detect this sign.

Key words: pupil, pupillary reflex, pupillography, pupillary defects

### Table 2. Cumulative total of subjects with visible initial constrictions

<table>
<thead>
<tr>
<th>Filter density (log units)</th>
<th>≥0.2 mm</th>
<th>≥0.3 mm</th>
</tr>
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<tbody>
<tr>
<td>3.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2.4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1.8</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>1.2</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>0.6</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

* Initial constrictions of filtered eye. With a 2.4 log filter over one eye, one subject had initial constrictions averaging more than 0.2 mm (but less than 0.3 mm) in amplitude during the alternating light test. At the 1.8 level, three more subjects had constrictions larger than 0.2 mm, for a total of four.

### References