Ophthalmologic Examination of Patients With Seasonal Affective Disorder, Before and After Bright Light Therapy

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• PURPOSE: We assessed the potential ocular hazards of bright light therapy for patients with seasonal affective disorder, after both short- and long-term treatment, and identified prospective patients with pre-existing ocular abnormalities.
• METHODS: Fifty patients with seasonal affective disorder received daily exposure to artificial light in the morning or evening for 30 minutes at an illuminance level of 10,000 lux (irradiant dose, .016 J/cm^2). Ophthalmologic examinations were performed before and after short-term treatment (two to eight weeks) and after three to six years of use during the fall and winter months. Over the four years of patient intake, the eye examination included subsets of the following tests: visual acuity, intraocular pressure, slit-lamp biomicroscopy, direct and indirect ophthalmoscopy, color vision, visual field, fundus photography, Amsler grid, ocular motility, pupillary reactions, contrast sensitivity, stereopsis, and the macular stress test.
• RESULTS: No ocular changes were detected after short-term treatment. Long-term treatment (three to six years) of 17 patients, with cumulative exposure durations of 60 to 1,250 hours, also resulted in no ocular abnormalities. • CONCLUSIONS: Light therapy yields about 75% clinical remissions. It is effective as an antidepressant and appears safe for the eyes. Current knowledge is insufficient to specify any definite ocular contraindications for bright light therapy, although we recommend that patients with pre-existing ocular abnormalities and those using photosensitizing drugs undergo treatment only with periodic Ophthalmologic examination.

THE THERAPEUTIC USE OF ARTIFICIAL BRIGHT light is a recently developed, yet already widely applied, treatment for the winter depression of seasonal affective disorder.[1] Patients with seasonal affective disorder regularly become depressed in late fall or winter and show spontaneous remission in spring and summer. Within the United States the syndrome is more prevalent at higher latitudes. Nationally, it is estimated that about 11 million people are affected at syndromal levels, and about 25 million people are affected at subsyndromal levels. Hallmark symptoms of the disorder include fatigue, increased sleep, carbohydrate craving, and dysphoric mood. When patients are undergoing light therapy, these symptoms are typically reduced or eliminated within one week.[2] In order to maintain remission, daily treatments are often continued throughout the fall and winter months. The antidepressant effect of light appear to be mediated by the eyes, not the skin.[3]

As originally studied at the National Institute of Mental Health[4] the treatment regimen used 2,500

lux (at eye level) of full-spectrum light designed to simulate the solar spectrum, including near and middle ultraviolet radiation. However, the eyes were partially shielded from ultraviolet light by a plastic diffusing screen. Daily treatment sessions usually required exposure for two hours or longer at this intensity level. Since 1987, however, we have used lamps that minimize ultraviolet radiation, with a raised illuminance of approximately 10,000 lux, and 30-minute treatment sessions.[5] Terman and associates[6] have described in detail potential ocular hazards of light treatment, particularly in association with preexisting ocular abnormality or concurrent use of photosensitizing drugs. A recent consensus report on the safety of light therapy devices concluded that no hazard has been identified "for a standard fluorescent lighting apparatus designed *to* produce 2,500 to 10,000 lux, given low levels of ultraviolet emission."[7] Remé, Menozzi, and Krueger[8] have proposed a set of standards for such illumination sources.

In the first clinical trials of light therapy, Rosenthal and associates[4] found no pretreatment to posttreatment ocular changes, on the basis of slit-lamp examinations, dark adaptometry, and fundus examinations. In more extensive comparisons between patients with seasonal affective disorder and normal controls, a large set of ophthalmologic tests yielded no statistically significant differences.[9] Lam and associates,[10,11] however, found small but significant reductions in visual sensitivity, as measured by electroretinogram b-wave amplitude[10] and electrooculographic Arden ratio,[11] in comparison with normal control subjects. These studies were designed to elucidate underlying ocular mechanisms involved in the pathogenesis of seasonal affective disorder and were not performed to screen for ocular abnormalities.

Whether all patients seeking bright light treatment should receive an ocular screening examination is a controversial matter.[12-14] Comprehensive ophthalmologic examination of patients with seasonal affective disorder has not yet been reported, and data that would form a basis for identifying patients at risk for ocular damage from light are lacking. Over the course of the present study, we selected and administered a set of basic diagnostic tests to identify pre-existing ocular abnormalities, to exclude patients from light treatment if the baseline examination indicated clini-

cally significant abnormality, and to evaluate retest results after an initial short-term treatment phase and after several years of treatment.

PATIENTS AND METHODS

RESEARCH VOLUNTEERS WERE SCREENED FOR prospective study according to National Institute of Mental Health diagnostic criteria for seasonal affective disorder[4] and the Diagnostic and Statistical Manual of Mental Disorders, third edition, revised (DSM-III-R)[15] (major depressive disorder, recurrent [296.3] or bipolar disorder not otherwise specified [296.7], both with seasonal pattern [winter type]). Patients entered clinical trials of light therapy between 1987 and 1991, after providing informed consent. Exclusion criteria included the following: (a) current treatment with psychotropic or photosensitizing medication, recent history of suicide attempt, panic or eating disorder unrelated to depression, or other DSM-1II-R axis I disorder; (b) current use of alcohol, marijuana, cocaine, or stimulant drugs, including diet pills; (c) ocular abnormality including corneal or retinal pathology, cataract, or narrow-angle or primary open-angle glaucoma; and (d) nonocular conditions including skin cancer, head injury, epilepsy, diabetes, or diseases requiring treatment with beta-adrenergic blockers. At the time of entry into the study, all patients met clinical severity criteria[16] for moderate to severe depression.

Before acceptance into the program, patients underwent a standard physical examination supplemented by electrocardiogram, urinalysis, and blood tests (complete blood cell count, including platelets, thyroid panel, cholesterol [high density lipoprotein, cholesterol/high-density lipoprotein ratio and triglycerides]), to rule out potentially complicating medical conditions.

Of 64 patients recruited into the study, two were excluded because of ophthalmologic indications. Because of scheduling constraints, five patients received only pretreatment ocular examinations and six received only posttreatment examinations (all with normal results). One patient refused a second examination with pupil dilation. To determine potential

short-term treatment effects, we analyzed the ocular results for the 50 patients who received both pretreatment and posttreatment ocular examinations during the year of entry into the study. This group included 13 men and 37 women, ages 18 to 62 years (mean ± S.D., 39.28 ± 11.38 years).

For long-term follow-up, all 30 (60%) patients who retained light boxes were contacted for reexamination in the fall of 1993. Of those patients, 17 returned for ocular examinations. Of the 13 who did not return, six had moved and could not be reached, four had discontinued use of the lights, and three were unable to schedule appointments. Thus, we examined 17 (85%) of 20 of the patients whom we could verify had continued with light therapy for three to six consecutive fall and winter seasons through 1993.

The pretreatment screening examination, included a medical history of systemic and ocular diseases, a review of potentially photosensitizing current medications, and notation of any ocular complaints. The Table shows the distribution of tests administered across the four years of the treatment study (1987 to 1991) and the follow-up examination (1993).[17] In the first two years, six basic tests were performed, accompanied by fundus photography of the central 30 degrees. Visual acuity was assessed by using the Snellen visual acuity chart with and without spectacle correction. Color vision was assessed using the American Optical or Ishihara plates. Static visual held was evaluated using the Humphrey automated perimeter (full-field 81-point screening test). Intraocular pressure was determined with Goldmann applanation tonometry, and the anterior segment was examined by slit-lamp biomicroscopy. After pupil dilation with tropicamide 1% and oxymetazoline hydrochloride 2.5%, the central and peripheral fundus was observed by direct and indirect ophthalmoscopy.

In the third and fourth years of the study fundus photography was discontinued as a cost-saving measure, because no abnormality had been detected by this means in previous patients. Visual field testing was discontinued in the fourth year because of the unavailability of an automated perimeter. Several tests were added to elucidate further potential changes of the central fundus and optic and oculomotor nerve function, as shown in the Table. A test of stereopsis was added to detect defects in visual acuity that might

be reflected in higher-order cerebral function. The Vistech 6000 chart was used to assess contrast sensitivity. Color vision was probed with more specificity by using the Farnsworth-Munsell 100 hue test and the Farnsworth panel D15. Additionally, patients completed a side effects checklist for assessment of potential subjective visual disturbances, based on the Systematic Assessment for Treatment Emergent Events,[18] which included eye irritation or swelling; blurred, double, or poor vision; photophobia; and the presence of other (unspecified) ocular problems.

Patients received the initial ocular examination during the pretreatment baseline period while they were depressed, with posttreatment evaluations after approximately two weeks of light treatment at 10,000 lux. In some cases, scheduling constraints delayed the posttreatment examination for up to two months, after completion of a second treatment phase (and thus, increased cumulative light exposure). For the follow-up examination after three to six years, a subset of seven diagnostic tests was used, as shown in the Table.

The time of day that light treatment sessions occurred was randomly assigned, in morning or evening intervals either between 5:30 and 7:30 AM or 5:30 and 7:30 PM. Daily 30-minute sessions were scheduled, at an illuminance of 10,000 lux. Treatment duration was approximately two weeks, followed by a withdrawal period of approximately ten days before switching to treatment at the alternate time of day.

The lighting fixture (Ultra-Brite 10,000 system, Medic-Light, Inc., Lake Hopatcong, New Jersey) was a metal box containing fluorescent lamps (using ultraviolet-attended, full-spectrum cool white, or triphosphor types) with a reflector and plastic diffusing screen mounted on a frame. It was set on a table top in an overhead frame at a 55-degree tilt from the horizontal, so that the light projected downward toward the face. This angular arrangement was designed to maximize illuminance while reducing glare and direct exposure to the eye, in contrast to vertical straight-on illumination. Patients were instructed to face the apparatus but not to look into it, concentrating instead on the illuminated table surface. A wide-angle digital illuminance meter measured light intensity to be approximately 10,000 lux at the level of the eyes. Reflection of light upward from a standard

INVENTORY OF TEST ADMINISTRATION*

	YEAR 1 (N = 17)	YEAR 2 (N = 13)	YEAR 3 (N = 12)	YEAR 4 (N = 8)	FOLLOW-UP EXAMINATION (N = 17)
Visual acuity (uncorrected and best-corrected)	Yes	Yes	Yes	Yes	Yes
Intraocular pressure	Yes	Yes	Yes	Yes	Yes
Slit-lamp biomicroscopy	Yes	Yes	Yes	Yes	Yes
Direct or indirect ophthalmoscopy	Yes	Yes	Yes	Yes	Yes
Color vision†	Yes	Yes	Yes	Yes	No
Visual field	Yes	Yes	Yes	No	No
Fundus photography	Yes	Yes	No	No	No
Side-effects checklist	No	Yes	Yes	Yes	No
Amsler grid	No	No	Yes	Yes	Yes
Ocular motility	No	No	Yes	Yes	Yes
Pupillary reactions	No	No	Yes	Yes	Yes
Contrast sensitivity	No	No	Yes	Yes	No
Stereopsis	No	No	Yes	Yes	No
Macular stress test	No	No	Yes	Yes	No
Color vision‡	No	No	Yes	Yes	No

*Yes indicates that the test was administered; no, that the test was not administered.
†American Optical or Ishihara Color Plates.
‡Farnsworth-Munsell D15 and 100 Hue.

white or black table surface did not markedly affect global illuminance.

In addition to the ocular examination, patients completed a usage-pattern questionnaire for which they retrospectively estimated the duration of light treatment per month across all years of the study.

RESULTS

DEPRESSION SCORES, WHICH WERE DETERMINED BY clinical raters without knowledge of the treatment condition (either morning or evening light or withdrawal) showed statistically significant pretreatment to posttreatment reductions. At baseline, the mean Hamilton depression scale score was 16.3 ± 4.2. After treatment it was 5.5 ± 5.5 (P = .0001 by two-tailed t-test for correlated samples). The atypical symptoms score (for hyperphagia, hypersomnia, fatigue, and the like) was 13.5 ± 4.6 at baseline; after treatment, it was reduced to 3.8 ± 4.6 (P = .0001), according to the rating scale criteria of Terman, Terman, and Rafferty[16] 38 (76%) of the 50 patients showed pretreatment to posttreatment score reductions of at least 50%, to scores of 7 or less on both Hamilton and

atypical scales (lowest posttreatment score of morning and evening conditions). This remission rate, categorically defined, matches or surpasses that of most previous studies that have used 2,500-lux morning light with two-hour daily exposures.[2,5]

At baseline, mild and moderate myopia (mild, 1 to 5 diopters; moderate, 6 to 10 diopters; and severe, greater than 10 diopters) was observed in 22 (44%) of 50 patients. One patient had anisometropic amblyopia (-10 diopters myopia). There was one patient with peripheral retinal degeneration (lattice and paving stone), two patients with peripapillary atrophy with tilted disk, and two patients with iris nevi and choroidal nevus (previously unknown to the patients). Two patients had old chorioretinal scars that were completely asymptomatic.

Three patients showed red-green color vision deficiencies, all of which had been previously diagnosed. In one patient an idiopathic preretinal fibrosis (cellophane maculopathy) was documented by fundus photography in both pretreatment and posttreatment tests. This patient had a mild color vision defect and altered Amsler grid perception secondary to the preretinal fibrosis. Neither condition is known to be exacerbated by exposure to light.

Visual field testing did not disclose any abnormalities that would be cause for exclusion from the study. Contrast sensitivity testing throughout the spatial frequency range of 1.5 to 18 cycles per degree disclosed 20 of 40 eyes (in 12 of 20 patients) with borderline high thresholds, but none of these were considered pathologic. Stereopsis testing disclosed no sensory anomalies other than preexisting amblyopia and myopia. Previous use of potentially photosensitizing psychotropic drugs (tricyclics, phenothiazines, or lithium) was noted for 20 patients (40%), with several of them having taken more than one such drug.

Over the course of this study, two patients were excluded from entry into the study on the basis of the baseline examination, in which uveitis and glaucoma were diagnosed.

None of the patients showed any pathologic change in their eyes that could be attributed to light therapy. Best-corrected visual acuity showed no detectable change in 43 of the patients, and small improvements that were seen in seven patients were within the range of test-retest reliability. Ocular motility was normal, as were direct and indirect pupillary reactions.

All patients showed Goldmann applanation intraocular pressures lower than 22 mm Hg, with symmetric readings to within 2 mm Hg seen in more than 90% of the patients. Pretreatment and posttreatment pressure varied by less than 4 mm Hg, which is within the expected range of test-retest variability, in all but four patients, who nonetheless were normal.

Ophthalmoscopic examination (direct or indirect) demonstrated sharp borders with symmetric cup/disk ratios of the optic nerve, all of which were within normal limits. Bilateral foveal reflexes were good and retinas were normal. Two patients had pre-existing retinal scars that did not change during treatment.

With the exception of the patient with preretinal fibrosis, assessment of macular function using the Amsler grid showed no scotoma nor metamorphopsia; the patient in question also showed no change from the pretreatment test. Furthermore, for the macular stress test administered to each eye, *t*-tests showed no significant changes in mean recovery time.

The results of color vision testing were normal for all but three patients known to have red-green deficiencies. The perception of color did not change after light therapy. That these patients responded well to light therapy is of potential theoretical interest in view of possible wavelength specificity in the response of patients with seasonal affective disorder.[19,20]

Contrast sensitivity testing disclosed 14 potentially abnormal eyes, three of which showed normal results at baseline before light treatment. All these eyes bordered on normal, however, and were not considered pathologic (for example, with a selective low-frequency deficit). By contrast, nine eyes that showed high threshold at baseline were normal after treatment. Statistically, we could detect no significant pretreatment to posttreatment change (McNemar test, chi-squared = 3.0, 1 degree of freedom, not significant). Visual fields, tested by automated perimetry, remained normal after treatment, except for the one patient whose defect was consistent with a retinal scar caused by earlier cryotherapy and who showed no posttreatment change.

Stereoscopic acuity was evaluated in 20 patients before and after light treatment. The test score did not change in 12 patients. Five patients showed an improvement of one to four points, and three showed a decrease of one to two points. Thus, 17 (85%) patients examined showed improvement or no change. There were no associated ocular changes detected in any of the patients who had reduced stereopsis scores, and it was judged that these results fell within the range of test-retest variability. Because of these negative results and the indirect aspect of the measure, which infers ocular function on the basis of cortical fusion of images from the two eyes, we subsequently dropped the test of stereopsis from the screening battery.

A summary of ocular symptoms reported on the self-rating checklist is shown in Figure 1. All symptoms showed mean severity levels on a scale of one to five (one indicates absent; five, severe) of less than two (absent to mild) at both baseline and posttreatment examinations. Surprisingly, reports of photophobia decreased significantly after treatment (P = .019). Reports of swollen eyes and blurred vision showed trends toward reduction (P = .058 and .096, respectively). Several patients reported worsening of eye irritation, poor vision, photophobia, or a combination of them. Most prominent among complaints was eye irritation (reported by four [11.8°o] of 34 patients). However, the complaints were not associat-
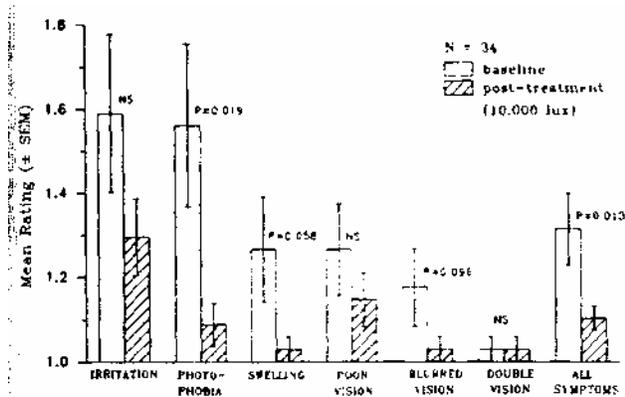
Fig. 1 (Gallin and associates). Severity of ocular symptoms (mean ± S.E.M.) as reported on the Systematic Assessment for Treatment Emergent Events[in] at baseline, that is, while depressed, and after light treatment.

ed with objective findings during ophthalmologic examinations, and the symptoms reported were always mild. Furthermore, these complaints were offset by an even larger proportion of patients (17.7%, six of 34) with reduced eye irritation after treatment. Overall, reports of ocular symptoms were significantly reduced at the posttreatment examination (P = .013). Whether this represents true improvement or a tendency toward fewer complaints while not depressed is unclear.

Among the 17 patients who returned for the follow-up examination, eight completed three consecutive years of fall and winter light usage, five completed four years, three completed five years, and one completed six years. On average, treatment was undertaken for 5.7 ± 2.2 months per year (range, two nine months). In addition to the fall and winter, three patients used the light during the spring and summer months when it rained or when the sky was overcast for several days. Figure 2 shows cumulative retrospective estimates of annual hours of light exposure. There were wide differences across patients, with cumulative exposure duration averaging 194.9 ± 141.3 hours (range, 49.1 to 567.8 hours). Corresponding cumulative irradiant doses were 6.2 ±4.5 J/cm^2 (range, 1.6 to 18.2 J/cm^2). The patient with maximum exposure received approximately 1,250 hours of light treatment over five years (40 J/cm^2), primarily because of frequent use of the apparatus as a desk lamp during the past two years.

There were no ocular abnormalities or clinically significant changes found in visual acuity, ocular motility, intraocular pressure, Amsler grid perception, and slit-lamp and fundus examinations.

DISCUSSION

THIS STUDY SYSTEMATICALLY SCREENED FOR OCULAR abnormalities in patients with seasonal affective disorder before and after bright light therapy, with follow-up after continued use for three to six years. No ocular abnormalities attributable to the treatment were found. Furthermore, although several patients reported slight increases in ocular irritation, response to the Systematic Assessment for Treatment Emergent Events questionnaire indicated a larger proportion of patients who noted reduced ocular irritation after light exposure. Other tests in the ophthalmologic examination failed to demonstrate clinically significant changes. Ocular status remained normal for all patients.

Patients with pre-existing ocular abnormalities (including cataract, glaucoma, cystic macular edema,
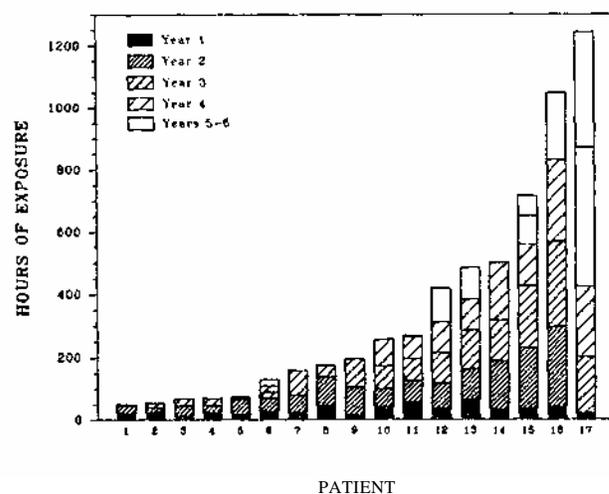

Fig. 2 (Gallin and associates). Cumulative light exposure duration (stacked histogram) for 17 patients who continued fall through winter treatments at 10,000 lux for three to six years. Durations for year 1 were determined from daily log sheets. Durations for later years were determined from patients' retrospective estimates of average weekly light exposure for each month of the year. Patient 17 did not use light treatment in year 2, but resumed it in years 3 to 6.

lattice and paving stone degeneration, early stage hypertensive retinopathy, and optic nerve head swelling) were excluded from the study on the basis of their medical history. Therefore, we cannot state whether such treatment would exacerbate the underlying condition. Current knowledge is insufficient to specify any definite ocular contraindications for bright light therapy, although we recommend that patients at potential risk undergo treatment only with ophthalmologic monitoring.

Mild to moderate myopia was found in 22 (44%) of the 50 patients, which is approximately twice the general prevalence in the United States population.[21] This finding has been confirmed in another study of patients with seasonal affective disorder, with 50% prevalence (Gorman CP, unpublished data presented at 5th Annual Meeting of the Society for Light Treatment and Biological Rhythms, June 1993). Whether myopia is linked to seasonal affective disorder, or the increased incidence reflects the particular age distribution or socioeconomic characteristics typical of these patients, is a matter for further inquiry.

The obvious hazards of exposure to ultraviolet light were minimized in this study by the use of lamps with very low ultraviolet emission levels. The SPX-35 lamp mounted in the 1O,000-lux light box configuration, for example, produces less than 0.01 u,W/cm^2/nm throughout the ultraviolet range, which is approximately two orders of magnitude lower than irradiance in the visible range. For cool-white light, the 10,000-lux, 30-minute light therapy regimen provides an irradiant dose of 0.016 J/cm^2 in one session,[5] equivalent to that of the earlier 2,500-lux, two-hour regimen. It must be acknowledged that, while not subject to close supervision of an experimental protocol, patients will often receive far higher doses (for example, the maximum of 0.09 J/cm^2 per day found for Patient 17; Fig. 2). Even at such an extreme level, however, we detected no ocular change after several years of exposure.

Patients using photosensitizing medications that might lead to acute ocular or dermal reactions were excluded from this study. Such medications absorb primarily in the UVA (320 to 400 nm) and UVB (290 to 320 nm) ranges, with some extending into the visible blue-green (400 to 550 nm) range.[5] Although the light sources used were selected for minimal ultraviolet radiation, we noted localized rashes in patients using Retin-A skin cream, as well as photoreactivation of herpes simplex blisters in one patient, presumably attributable to residual ultraviolet exposure, which quickly resolved by use of a topical sunblock. Thus, additional short-wavelength filtering or use of sun blocks and ultraviolet- and blue-blocking spectacles may be an important safety pre-caution for patients using bright light therapy while taking photosensitizing medications.

The advisability of ophthalmologic examinations for patients undergoing bright light therapy has been debated in the literature. Vanselow and associates[12] described a study candidate for whom a pre-existing perimacular pigment epithelial scar was discovered in initial screening and who was denied light treatment Waxler and associates[14] questioned the need for such exclusion, because the light is not known to cause or exacerbate retinopathy. They argued that because the light levels that are used for therapy are far lower than naturally occurring outdoor light, which can reach approximately 100,000 lux, routine ophthalmologic screening is not necessary. Two of us responded, however, that such examinations are needed to reduce the likelihood that unknown pre-existing ocular abnormalities would subsequently be attributed to the light.[13] Furthermore, light exacerbation of degenerative processes in the retina, especially that of age-related maculopathy, remains a topic of investigation both clinically and experimentally,[22,23] and light-induced retinal lesions have been observed both in humans[24] and animals.[25]

The argument that light therapy poses no more hazard than does normal outdoor light has often been used to downplay the potential risk. However, many individuals are normally exposed only briefly to outdoor light,[26] and the treatment procedure can be different from normal patterns of exposure to light. Furthermore, the geometric arrangement of the lighting fixture, in close proximity to the patient and with a relatively inescapable field of illumination, contrasts with outdoor exposure conditions in which head and body movement create a more varied exposure pattern. We have found several patients for whom the daily light-therapy session entails exposures greatly exceeding the spontaneous pattern either indoors or outdoors. Even though we have identified no adverse

treatment effects either during the initial year or at the three- to six-year follow-up examinations, longer-term sequelae cannot he ruled out. Cumulative photoinduced retinal changes may take decades to reach a pathologic threshold, and it may he difficult to distinguish such cases from, for example, age-related degenerative changes.

Although our exclusion criteria were strict, in light of the present results, exclusions might now be narrowed, providing access to patients with ocular abnormalities who might nonetheless benefit from light therapy without increased ocular risk. For example, patients with suspected glaucoma might receive such treatment, although patients with progressive retinal diseases, such as diabetic retinopathy, macular degeneration, or retinitis pigmentosa, would continue to be excluded. Even then, however, if a patient cannot tolerate or has not responded to antidepressant medications, then bright light treatment might be administered in conjunction with ophthalmologic monitoring. A promising alternative, at a far lower dose, is low-intensity dawn light simulation, which appears efficacious as a bedside treatment during the final hours of sleep.[27]

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