

Research Articles

BRIGHT LIGHT AUGMENTS ANTIDEPRESSANT EFFECTS OF MEDICATION AND WAKE THERAPY

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Inpatient studies have suggested that bright light therapy can be used to sustain the antidepressant effects of wake therapy (sleep deprivation). In an outpatient trial, a half night of home wake treatment was followed by 1 week of light treatment. All subjects had Major Depressive Disorders according to DSM-IV criteria and were receiving concomitant antidepressant medication. Subjects were randomly assigned to receive either 10,000 lux bright white light for 30 min between 6 and 9 AM or dim red (placebo) light at a comparable time. Seven subjects completed treatment with bright white light and six completed treatment with placebo. On the Hamilton Depression Rating Scale (HDRS17, SIGH-SAD-SR version), the group receiving bright light improved 27% in 1 week ($P=0.002$). The group receiving placebo did not improve, except for one outlier. The benefit of bright light was significant compared to placebo with removal of the outlier ($P<0.025$). Depression and Anxiety 16:1–3, 2002.

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INTRODUCTION

One half night of wake therapy can produce an immediate antidepressant benefit, especially when the patient remains awake in the second half of the night [Wu and Bunney, 1990; Wirz-Justice and van den Hoofdakker, 1999]. (The term “wake therapy” has been suggested to avoid the negative cognitive connotations of the term “sleep deprivation” when waking is arranged for treatment.) Unfortunately, patients commonly relapse after a full night’s sleep, so many investigations have searched for medications or other methods of maintaining the rapid benefit that patients may receive. In an inpatient study, Neumeister et al. [1996] found that excellent responses to wake therapy can be maintained if the patient receives bright light treatments every morning thereafter. A 35% improvement in depression as compared to dim light control treatment was observed at the end of a week. This benefit has recently been replicated by Bloching et al. [2000] and Fritzsche et al. [2001]. We examined whether this antidepressant benefit could be obtained in an outpatient setting.

METHODS

Thirteen patients of the University of California, San Diego (UCSD) outpatient clinic, eleven women and two men, gave written informed consent for this study, under supervision of UCSD’s institutional review board. Their mean age was 44 years (range 26–56).

All were diagnosed as having Major Depressive Disorder according to DSM-IV criteria, and none had seasonal trait. Subjects were studied throughout the year. All were receiving standard antidepressant medications and supportive psychotherapy, some for many months, but had not yet experienced a satisfactory response. Each patient had a primary psychiatrist outside the research team. Medications and psychotherapy were maintained during the research protocol. The protocol did not alter standard therapy in any way, and light was used only to augment existing treatment. The primary psychiatrist was free to intervene at any time during the study as prior to the study. Data on medications is presented in Table 1. Data on changes in psychotherapeutic intervention were not available. However, there was no indication that any significant change in therapeutic approach occurred with any of the subjects.

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TABLE 1. Individual medications regimens at time of study

| Treatment | Medication | Comments |
|--------------|--|---|
| Bright white | Paroxetine 60 mg Venlafaxine 75 mg | Tapering off paroxetine |
| Bright white | Parnate 60 mg Carbamazepine 600 mg Methylphenidate 5 mg | Prescribed for more than 2 months |
| Bright white | Paroxetine 30 mg Methylphenidate SR 40 mg | Prescribed for more than 2 months |
| Bright white | Sertraline 100 mg Bupropion 150 mg | Prescribed for 2 months |
| Bright white | Paroxetine 20 mg | Prescribed for more than 2 months |
| Bright white | Sertraline 100 mg | Prescribed for more than 2 months |
| Bright white | Paroxetine 60 mg | Prescribed for more than 2 months |
| Dim red | Paroxetine 40 mg | Prescribed for more than 2 months |
| Dim red | No Meds | Recent trial of Serzone not tolerated, stopped at 50 mg. Prior trial of nortriptyline, 10 mg |
| Dim red | Venlafaxine 400 mg Bupropion 300 mg Trazodone 300 mg Diazepam 10 mg Valproate 250 mg | Prescribed for more than 2 months |
| Dim red | Bupropion 400 mg Trazodone 25 mg | Prescribed for more than 2 months |
| Dim red | Fluoxetine 50 mg | Prescribed for more than 2 months |
| Dim red | Bupropion 300 mg | Prescribed for more than 2 months |

At the start of the study, a baseline Hamilton Depression Rating Scale (HDRS17) was completed, using the SIGH-SAD-SR [Williams et al., 1990], which contains a self-rating form of the HDRS17. Each patient then agreed to awaken at 3:00 AM while at home and to remain awake for the remainder of the night. To monitor compliance, patients were asked to telephone a telephone answering machine every half hour until beginning light treatment. That morning patients commenced experimental light treatment which continued for six additional mornings. The light treatment was scheduled for 30 min between 6 and 9 AM, and consisted of exposure to a light box at eye level from a distance of 18 inches. Patients were randomly assigned to receive either 10,000 lux bright white light from an Apollo Lighting Systems Brite Lite III or 100 lux dim red placebo light from a comparable box with a dark red filter. At the end of the 1-week treatment, the depression self-ratings were repeated.

RESULTS

Initial HDRS17 scores ranged from 10 to 41, with a mean of 21.6, and were not significantly different between those assigned to bright or placebo light (Table 2). The bright-light-treated group improved 27% on HDRS17 at the end of the week ($P = 0.002$).

The placebo group improved 20%, but the gain was not significant. The placebo group improvement was

due entirely to one outlier, whose HDRS17 self-rating dropped from 32 to 5, even though her therapist felt that she did not improve. Because the change score for this subject was an outlier 2.58 SD from the mean change score, and it skewed the distribution, this

TABLE 2. Hamilton depression rating scale (HDRS17) scores

| Pre | Post |
|--------------|------|
| Bright light | |
| 41 | 33 |
| 11 | 5 |
| 19 | 7 |
| 25 | 23 |
| 24 | 16 |
| 31 | 30 |
| 17 | 8 |
| Control | |
| 17 | 15 |
| 18 | 17 |
| 18 | 27 |
| 18 | 19 |
| 32 | 5 |
| 10 | 7 |

This research was performed on human subjects and complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and the standards established by the UCSD Institutional Review Board and the National Institutes of Health.

subject was excluded in computing HDRS17 change scores from baseline to the end of the 1-week treatment. Excluding this outlier, the placebo group did not improve, and the benefit of bright light was significant compared to placebo ($t=2.82$, $P<0.025$, two-tailed). The group difference was not significant if the outlier was retained. Mann-Whitney (nonparametric) tests of the change scores were conducted. Including the outlier resulted in $P=0.151$, and when the outlier was excluded, $P=0.028$. The effect size, eta squared, was $\eta^2=0.896$ and $\eta^2=0.892$, respectively.

DISCUSSION

Patients with major depressive disorders who were treated with the combination of bright light, wake therapy, and continuing medication improved 27% within 1 week. The response was especially gratifying since a number of the patients had not been remitting with antidepressant medication and psychotherapy, and the placebo group did not improve within the 1-week time span. Medication changes did not appear to contribute to this difference. The treatment group had six out of seven subjects with stable medication regimen for 2 months or more and the placebo group had five out of six subjects with stable medication regimen for 2 months or more and one subject on no medication (Table 1). The benefits achieved by outpatients in the home were comparable to those achieved by inpatients in the study by Neumeister et al. [1996] and replications. [Bloching et al., 2000; Fritzsche et al., 2001].

The magnitude of benefit by which bright light, wake therapy, and medication exceeded the benefits of placebo, wake therapy, and medication was 27% within 1 week. This is a superior response, compared to the benefits of antidepressant drugs, which produce relative benefits of only 8–11% contrasted to placebo after 8 weeks [Khan et al., 2000]. It appears that bright light combined with wake therapy and medication might produce a much better antidepressant response much more rapidly than our available antidepressant drugs. However, despite powerful effects shown here,

until more comparative studies are done, we cannot be certain of this conclusion. Possibly, bright light alone may produce an excellent antidepressant response in 1–4 weeks, but the best responses seem to occur in combination with medication and wake therapy [Kripke, 1998].

An important limitation of this study was the small number of subjects, since the study had to be terminated before planned subject accrual, due to administrative problems. A second limitation was that the contrast between bright light and placebo would not appear statistically significant without removal of an outlier. A third limitation is the lack of follow-up beyond 1 week. Currently, we are attempting a new trial with 4 weeks of bright light treatment.

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