

Bright Light Therapy and/or Imipramine for Inpatients with Recurrent Non-Seasonal Depression

Jan Prasko, Jiri Horacek, Jan Klaschka, Jirina Kosova, Ivana Ondrackova & Jiri Sipek

Head of the Psychiatric Centre Prague: Prof. MUDr. Cyril Höschl, DrSc.
Psychiatric centre Prague, Ustavni 91, Prague – 8, 181 03 Czech Republic
3rd Medical faculty Charles University Prague, Centre of Neuropsychiatric Studies

Correspondence to: Jan Prasko, M.D., Ph.D.
Psychiatric centre Prague, Ustavni 91, Prague – 8, 181 03 Czech Republic.
TEL +420-2-66003 100
FAX + 420-2-66003366
E-MAIL: prasko@pcp.lf3.cuni.cz

Submitted: January 19, 2002
Accepted: January 23, 2002

Key words: **Major depressive disorder; inpatients; bright light therapy; imipramine; combination, clinical trial**

Neuroendocrinology Letters 2002; 23:109–113 pii: NEL230202A04 Copyright © Neuroendocrinology Letters 2002

Abstract

INTRODUCTION: The aim of a double-blind study was to assess the efficacy of bright light therapy and/or imipramine in the treatment of inpatients suffering with recurrent non-seasonal major depressive disorder.

METHOD: 34 in-patients with DSM-III-R diagnosis of major depressive disorder, recurrent type, were randomly allocated into 3 treatment groups. After 4-day washout period with baseline assessment they underwent 3 weeks of different types of treatment:

- a) Group A: bright light therapy (5000 lux from 6–8 a.m.) and imipramine 150 mg/day.
- b) Group B: bright light therapy (5000 lux from 6–8 a.m.) and imipramine-like placebo.
- c) Group C: dim red light (500 lux from 6–8 a.m.) and imipramine 150 mg/day.

Outcome measures included weekly Hamilton Psychiatric Rating Scale for Depression, Clinical Global Impression Scale, Montgomery and Asberg Psychiatric Rating Scale for Depression and Beck Depression Inventory.

RESULTS: Patients of all three groups improved significantly. The improvement of the patients of group B treated with bright light therapy plus placebo was superior to the other two groups, but not significantly.

CONCLUSION: Bright light therapy can be effective in the treatment of non-seasonal major depressive disorder.

Introduction

Depression is a common disorder, with serious consequences for a high proportion of patients. Indeed, it is estimated that 2.6 – 6.2% of the general population experience depression in any given year [1] and that 15% of those who develop severe and recurrent illness eventually take their own lives [2]. Unfortunately, although ranges of effective antidepressant agents are available, many require an administration period of at least 2 weeks, and some up to 4 weeks, before a therapeutic effect is seen [3]. Bright light is a unique treatment method, which is effective and well tolerated and has an early onset of action, in the treatment of patients with Seasonal affective disorder [4, 5]. Some studies reported an antidepressant effect of bright light also in non-seasonal depression (non-SAD) [6, 7, 8]. However, the reports concerning the effect of a short-term administration of bright light on non-SAD depression are controversial. The aim of our double-blind study was to compare the effect of a three week bright light therapy and/or imipramine in the treatment of inpatients suffering with recurrent non-seasonal major depressive disorder.

Subject and Methods

Patients admitted to the clinical psychiatric inpatient department of the Psychiatric Centre Prague were screened by an experienced psychiatrist for meeting DSM-III-R diagnostic criteria for recurrent major depressive disorder [9]. The diagnosis was independently confirmed by two independent experienced psychiatrists.

The inclusion criteria:

- 1) Age 20–60 years.
- 2) Meeting the DSM-III-R diagnostic criteria for recurrent major depressive disorder of moderate or severe type (296.32 and 296.33) without seasonal pattern.
- 3) At least 2 episodes of major depression in life time, and at least one episode of major depression during the last 2 years previous the current episode; at least one episode in another season than the current one.
- 4) Total score of the 21-item Hamilton Psychiatric Rating Scale for Depression [10] higher than 20.
- 5) Written informed consent.

Exclusion criteria:

- 1) The presence of any of the following mental conditions:
 - a. Bipolar depression
 - b. Panic disorder.
 - c. Alcoholism or drug abuse.
 - d. Antisocial personality disorder.
 - e. Histrionic personality disorder.
 - f. History of schizophrenia.
 - g. Organic brain impairment.
 - h. Mental retardation.

- 2) Presence of specific physical illness or medical contraindications for using imipramine; endocrine disease in history.
- 3) Pregnancy.
- 4) Treatment by drugs causing depression in the last month.
- 5) Eye diseases (such as the aphakic condition, retinal diseases, inflammatory diseases, glaucoma, cataracts and optic nerve disease).

Patients were randomly assigned into three groups with different treatment strategies. Each type of treatment was administered for 21 consecutive days after 4 days of a placebo period. The groups were:

- a) Group A: bright light therapy (5000 lx from 6–8 a.m.) and imipramine 150 mg/day.
- b) Group B: bright light therapy (5000 lx from 6–8 a.m.) and imipramine-like placebo.
- c) Group C: dim red light (500 lx from 6–8 a.m.) and imipramine 150 mg/day.

Light specifications:

- a) Bright-light: 5 000 lx (14 cool white fluorescent tubes, DAYLIGHT Tesla) on a portable box.
- b) Dim red-light: 500 lx (3 cool white fluorescent tubes, DAYLIGHT Tesla and red filter), on a portable box.

Main outcome measures:

Outcome measures included baseline and weekly evaluation by 21-item Hamilton Psychiatric Rating Scale for Depression (HAM-D) [10], Clinical Global Impression Scale (CGI) [11], Montgomery and Åsberg Psychiatric Rating Scale for Depression (MADRS) [12], and Beck Depression Inventory (BDI) [13]. We used Czech version of scales [14]. HAM-D, CGI and MADRS were rated by an independent psychiatrist.

Statistical analysis:

The data were analysed by the analysis of variance with repeated measures (ANOVA; Software BMDP) [15]. For each scale a separate analysis was performed comparing the raw scores in the three groups during the four measurements periods. The parameter of major interest was the interaction between the treatment groups and time.

Results

Thirty-four newly admitted in-patients with mean age 42.6 (SD=10.3), 12 male and 22 female were randomly allocated into 3 treatment groups. Twenty-nine patients completed the study and there were 5 drop-outs (group A:11 finished and 2 drop-outs, group B: 9 finished and 2 drop-outs, group C:9 finished and 1 drop-out) (Table 1). There are no significant differences in the demographic characteristics of patients (age, gender, numbers of previous depressive episodes, duration of illness, education, employment) between the groups. The drop-outs did not stand out as to demographic variables or the severity of illness. All drop-outs appeared during the first week of study. Two pa-

tients (one of the group A and one of the group B) developed hypomania. They remained euthymic for a week after discontinuing bright light therapy. Two patients (one of the group A and one of the group C) dropped out due to adverse side effects of the treatment (both suffered from typical anticholinergic effects of imipramine), and one patient of the group B dropped out due to non-compliance.

Table 1. Characteristics of patients completing the study

	N	mean age	gender male:female	mean number of previous episodes of depression
Group A	11	41.0 ± 9.3	3:8	4.0 ± 1.4
Group B	9	44.1 ± 11.6	4:5	3.5 ± 0.8
Group C	9	43.2 ± 10.9	3:6	3.8 ± 1.2
Total	29	42.6 ± 10.3	10:19	3.8 ± 1.2

Table 2: Characteristics of patients completing the study

The analysis of variance with repeated measures for each scale separately showed statistically significant changes over time in all three treatment groups (HAMD $p < 0.01$; BDI $p < 0.01$; MADRS $p < 0.01$ and CGI-severity of illness $p < 0.01$). The plot of mean group scores against time showed that the improvement in the patients of the group B (bright light therapy plus placebo) was superior to that of the group A (bright light and imipramine) in BDI (two-way ANOVA: $p < 0.05$), CGI ($p < 0.005$), HAMD ($p < 0.05$), MADRS ($p < 0.01$) (Table 2). There were no statistical differences in the outcome of treatment between the groups B (bright light therapy plus placebo) and C (imipramine and dim red light) in any of the ratings except for BDI in favour of the group B (ANOVA: $p < 0.05$). Using the criteria of Terman et al. [5], who defines the response to bright light therapy by a 50% reduction in HAMD to a value less than 8, we found that 4 patients (36.4%) responded to treatment in the A group, 6 (66.7%) responded in the B group, and 3 (33.3%) responded in the C group.

Table 2. Median BDI, HAMD, CGI and MADRS ratings in three treatment groups

Outcome Measure	Period	A (n=11) (BLT+IMI)		B (n=9) (BLT+PLAIMI)		C (n=9) (DRL+IMI)		Two-way analysis of variance with repeated measures		
		Mean	SD	Mean	SD	Mean	SD			
BDI	Day 0	32.9	11.5	34.2	10.3	31.8	12.2	A v. B v. C:	F=2.25	$p < 0.05$
	Day 7	30.5	11.4	23.1	13.3	29.7	13.2	A v. B:	F=3.10	$p < 0.05$
	Day 14	26.2	14.4	19.6	10.8	27.0	12.7	B v. C:	F=2.86	$p < 0.05$
	Day 21	24.8	14.7	15.0	9.9	22.3	10.9	A v. C:		n.s.
HAMD	Day 0	23.0	6.4	23.1	3.6	24.7	3.8	A v. B v. C:		n.s.
	Day 7	21.0	7.3	15.7	7.8	22.6	6.3	A v. B:	F=3.31	$p < 0.05$
	Day 14	15.5	8.3	14.0	7.7	18.7	8.6	B v. C:		n.s.
	Day 21	17.0	11.2	8.7	5.8	13.0	7.9	A v. C:		n.s.
CGI	Day 0	4.36	0.92	4.67	0.71	4.33	0.71	A v. B v. C:	F=3.42	$p < 0.005$
	Day 7	3.82	1.33	3.78	1.20	3.89	0.93	A v. B:	F=5.54	$p < 0.005$
	Day 14	3.18	1.17	3.22	1.09	3.22	0.83	B v. C:		n.s.
	Day 21	3.45	1.51	2.00	1.00	2.67	0.87	A v. C:		n.s.
MADRS	Day 0	27.6	7.9	26.2	5.8	27.1	5.6	A v. B v. C:	F=2.52	$p < 0.05$
	Day 7	24.1	9.2	18.0	9.5	22.1	6.8	A v. B:	F=4.36	$p < 0.01$
	Day 14	16.7	8.4	17.1	10.2	17.2	8.5	B v. C:		n.s.
	Day 21	18.4	12.0	8.7	5.4	12.4	7.9	A v. C:		n.s.

PLAIMI = imipramine-like placebo

BLT = bright light therapy

IMI = imipramine

DRL = dim red light

A = group A

B = group B

C = group C

v. = versus (comparing with)

BDI = Beck Depression Inventory

HAMD = 21-item Hamilton Psychiatric Rating Scale for Depression

CGI = Clinical Global Impression Scale – Severity of Illness

MADRS = Montgomery and Asberg Psychiatric Rating Scale for Depression

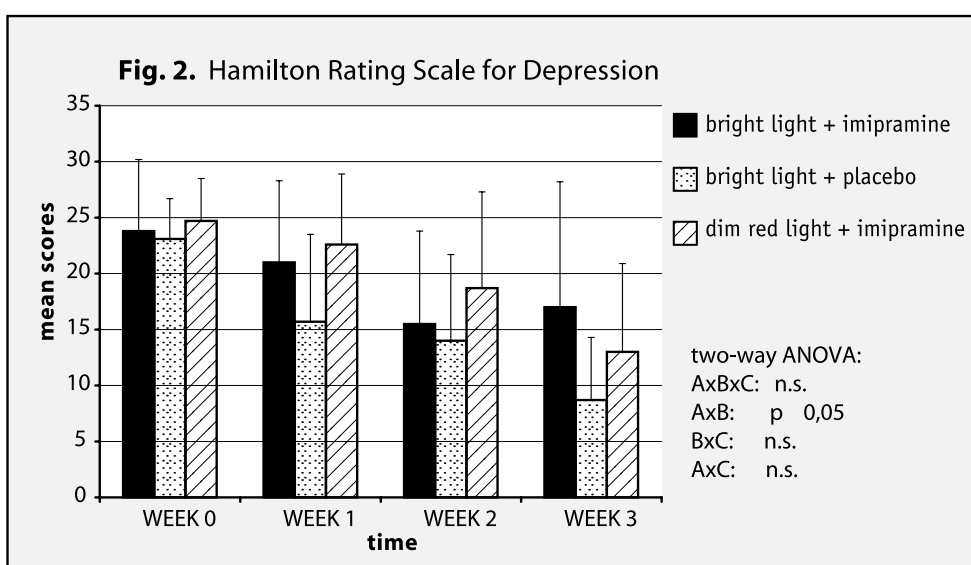
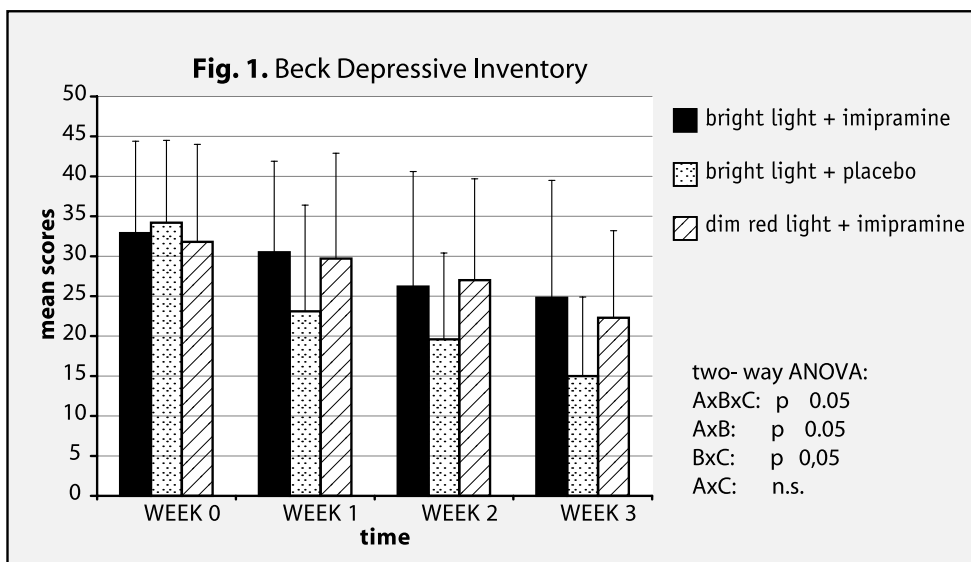


Fig. 1. Beck Depression Inventory
 Fig. 2. Hamilton Rating Scale for Depression

Discussion

The data suggest that the 3 weeks application of morning bright light without additional pharmacotherapy could be an effective short-term treatment for patients with recurrent unipolar major depressive disorder without seasonal pattern. The efficacy of bright light therapy alone was comparable with that of the imipramine treatment, and surprisingly better than the combination of bright light and imipramine. Our present results corroborate and extend previous findings about the efficacy of bright light therapy in non-seasonal depressive disorder [7, 8]. Why the combined therapy is less effective than each treatment alone is a question open to further investigation. This result contrasts with our previous findings which suggested an acceleration of the effect of antidepressants by using phototherapy in endogenous depression. In that earlier study we used, however, other antidepressants, mostly amitriptyline. It is possible that different results we obtained now were due to a different effect of distinct an-

tidepressants used in combination with the light treatment. We cannot rule out a placebo effect. Possible placebo effect of bright light therapy was described by Eastman [16] in patients with seasonal affective disorder. However, if the efficacy of treatment by bright light and placebo was mainly due to a placebo effect of bright light, why we did not observe this in the group treated by bright light and imipramine? Another problem is that dim light is not physiologically active in humans. In such instances red light with intensity 500 lux would not be an appropriate light-placebo control. To clarify these questions further long-term, follow-up trials, including an untreated (i.e. negative) or a true placebo control groups are needed.

Acknowledgment

Supported by grant CNS LN00B12 MSMT CR and by grant IGA: 870-2.

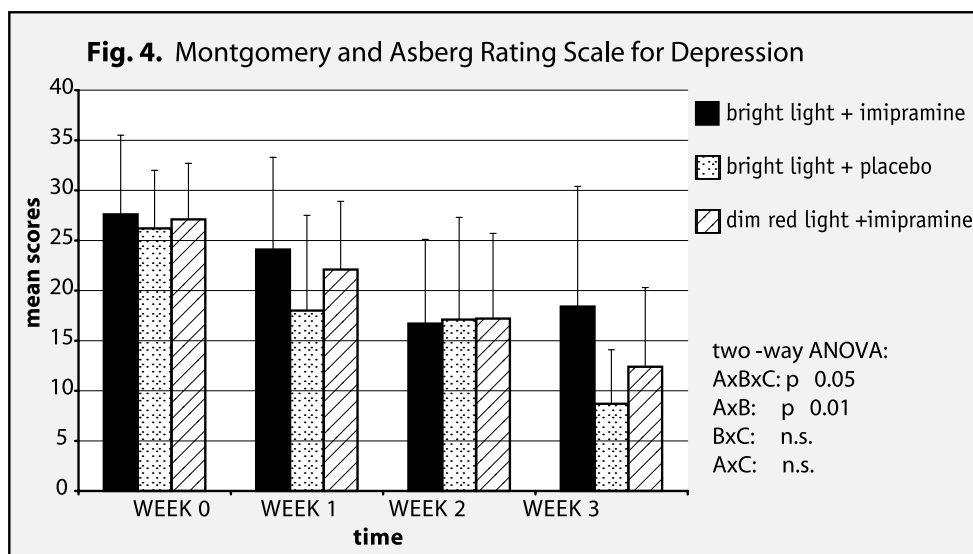
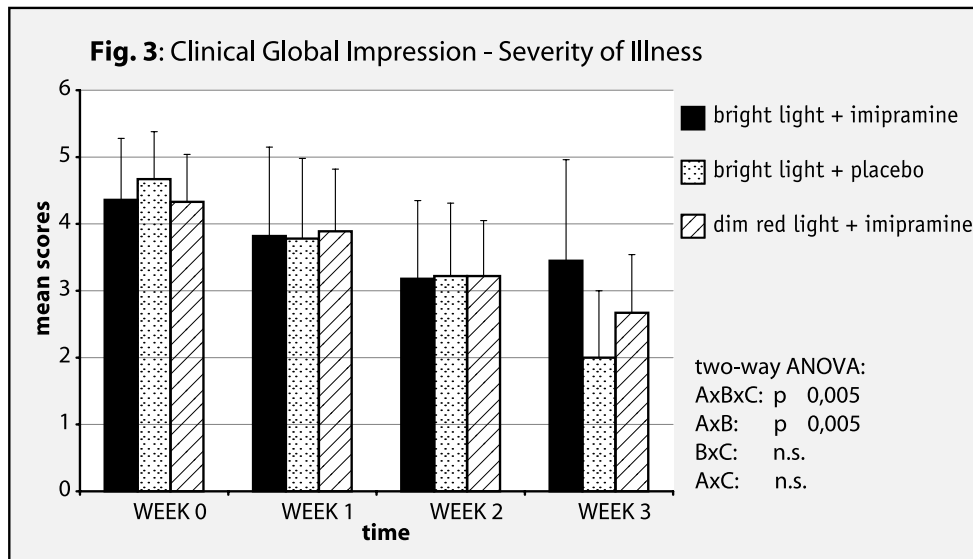


Fig. 3. Clinical Global Impression – Severity of Illness

Fig. 4. Montgomery and Åsberg Rating Scale for Depression

REFERENCES

- 1 Angst J. Epidemiology of depression. *Psychopharmacol* 1992; **102**:S71–S74.
- 2 Montgomery SA. Suicide and antidepressants. *Drugs* 1992; **43**(suppl 2):24–31.
- 3 Speight TM, Holford NHG, editors. *Avery's Drug Treatment*, (4th edn). Adis International Ltd, New Zealand; 1997.
- 4 Rosenthal NE, Sack DA, Gillin JC et al: Seasonal affective disorder: A description of the syndrome and preliminary findings with light therapy. *Arch Gen Psychiatry* 1984; **41**:72–80.
- 5 Terman M, Terman JS, Quitkin F, McGrath P, Stewart J, Rafferty B. Light therapy for seasonal affective disorder: A review of efficacy. *Neuropsychopharmacology* 1989; **2**:1–22.
- 6 Dietzel M, Saletu B, Lesch O, Sieghart W, Schjerve M. Light treatment in depressive illness: Polysomnographic, psychometric, and neuroendocrinologic findings. *Eur Neurol* 1986; **25**(suppl):93–103.
- 7 Prasko J. *Fototerapie a cirkadianni rytmy u depresivnich poruch* (dissertation) (Phototherapy and circadian rhythms in depressive disorders.) (In Czech with English abstract): Prague, Charles University; 1991.
- 8 Kripke D, Mullaney D, Klauber M, Risch S, Gillin C. Controlled trial of bright light for nonseasonal major depressive disorders. *Biol Psychiatry* 1992; **31**:119–134.
- 9 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. Third Edition-Revised. Washington, DS; 1987.
- 10 Hamilton M. Development of a Rating Scale for Primary Depressive Illness. *Brit J Soc Clin Psychol* 1967; **6**:278–296.
- 11 Guy W (Ed.). *ECDEU Assessment Manual for Psychopharmacology* revised Maryland: National Institute of Mental Health; 1976.
- 12 Montgomery SA, Åsberg M. A New Depression Scale Designed to be Sensitive to Change. *Brit. J. Psychiatry* 1979; **134**:382–389.
- 13 Beck AT, Beamesderfer A. Assessment of Depression: The Depression Inventory. In: *Psychological Measurements in Psychopharmacology* 1974; **7**:151–169.
- 14 Filip V, David I, Jirak R, Posmurova M. *Prakticky manual psychiatrickych posuzovacich stupnic* (Comprehensive manual of psychiatric rating scales). VUPs, Prague 1985.
- 15 Dixon WJ, editor. *BMDP Statistical Software Manual*. Version 7.0. Berkeley: University of California Press. Wiley & Sons Ltd; 1992.
- 16 Eastman C. What the placebo literature can tell us about phototherapy for SAD. *Psychopharmacol Bull* 1990; **26**:495–504.