Sleep deprivation response in seasonal affective disorder during a 40-h constant routine

Peter Graw[a], Hans-Joachim Haug[a], Georg Leonhardt[b], Anna Wirz-Justice[a],*

[a]*Chronobiology and Sleep Laboratory, Psychiatric University Clinic, Wilhelm Klein Strasse 27, CH-4025 Basel, Switzerland*
[b]*Neurological Clinic and Outpatient Clinic, 45122 Essen, Germany*

Abstract

Background: There are no controlled studies investigating the response of patients with seasonal affective disorder (SAD) to a total sleep deprivation (SD). *Methods*: The clinical response to SD of patients with SAD in winter was investigated under the stringently controlled conditions of a 40-h constant routine protocol. *Results*: 52% of the SAD patients ($N = 11$ women) improved, using a mean of a multiple ratings. This is in the range of response found for non-seasonal major depression. In contrast, controls ($N = 8$ women) showed less improvement of mood (29%). *Conclusion*: SAD patients respond to SD as do non-seasonal major depressives. The best discrimination of response was obtained in an observer rating (Clinical Global Impression: global severity improvement), and the morning values of two different self ratings (v. Zerssen depression scale, 100 mm VAS with the criterion of ≥ 10 mm improvement). *Limitation*: A more reliable estimate of the SD response rate in SAD patients would require a larger group. *Clinical Relevance*: SAD patients do not differ from other subgroups of major depression in their response to SD, and therefore this is an additional treatment option to light therapy. © 1998 Elsevier Science B.V.

Keywords: Seasonal affective disorder; Sleep deprivation; Response criteria

1. Introduction

Total sleep deprivation (SD) induces a rapid, albeit mostly short-lasting improvement in about 60% of depressed patients independent of diagnostic categories (reviewed in Kuhs and Tölle, 1986; Wu and Bunney, 1990; Leibenluft and Wehr, 1992; Rudolf, 1996). Whether patients suffering from seasonal affective disorder (SAD) also respond to SD is still an open question, since there are no studies addressing this issue. In these patients, there is a consensus that bright light is the treatment of choice (Lam et al., 1997). Bright light is not

necessary for the SD response in major depression (Wehr et al., 1985), nor does it potentiate the SD effect (van den Burg et al., 1990), although it appears to prevent the relapse after recovery sleep (Neumeister et al., 1996). There are some hints that SAD also profit from SD (Wehr et al., 1985).

The aim of this paper is to test whether SAD patients, as other major depressives, respond to SD. We were able to study SD response in depressed SAD patients whose circadian rhythms were investigated under the rigorously controlled conditions of a constant routine (described below). Additionally, the multiple ratings carried out permitted testing different criteria for determining clinical response.

2. Methods

The duration of the study was 4 years, each winter half year from October to March. Women diagnosed as suffering from SAD (DSM-III-R; American Psychiatric Association, 1987) with a depression score ≥ 13 (Hamilton Rating Scale for Depression, 21 item version HAM-D; Hamilton, 1967) and age-matched control women who were medically screened and had no prior psychiatric illness, participated in a "constant routine" protocol. The constant routine (CR) is a design to investigate endogenous circadian rhythms without environmental and behavioral "masking" (Czeisler et al., 1989). This means that subjects are kept in a constant posture (sitting at 45° in bed), continuously awake for 40 h in a controlled environment (temperature 22°C, humidity 60%, light < 80 lux). They receive isocaloric snacks at 2 h intervals (details of the experimental protocol in Brunner et al., 1996). The 40 h CR includes a night of total SD. Since subjects remain awake throughout, the differences from a conventional clinical SD are the controlled wakefulness on the day before and day after SD, lack of motor activity, and equispaced small isocaloric meals instead of the usual 3 meals, as well as constant environmental conditions without time cues.

The instruments used to document clinical change were:

- Each morning an observer rating: the Clinical Global Impression (CGI; global severity improvement [GSI] and depression severity improvement [DSI]; CGI, National Institute of Mental Health, 1976). In two cases where the CGI was not documented, changes in the HAM-D without items 4,5,6 and 18 were used.
- Every 6 h a validated self-rating scale for depression (DS/DS'; von Zerssen and Koeller, 1976).
- Half-hourly self-rating of mood on a Visual Analogue Scale (VAS: 0 mm = worst possible depressed mood, 100 mm = best possible mood; Aitken, 1969), a scale which has been tested for reliability and validity in its German version (Fähndrich and Linden, 1982).

For the two latter measurements, the morning (11 h) and evening ratings (20 h) were compared.

Different criteria for SD response were tested:

- an improvement of any degree (CGI, HAM-D, DS/DS' and VAS > 0 mm)
- an improvement of ≥ 10 mm (VAS)
- positive regression in a linear trend (VAS)

These criteria were chosen since Haug and Fähndrich (1986) had previously shown that the response rate to SD in a group with major depression ($N = 76$) was 40% when the criterion of VAS ≥ 10 mm improvement was used, and was 61% using the criterion of any improvement at all (> 0 mm).

For the relapse after a night of recovery sleep the same criteria as for response were used but with the opposite signs.

To judge a single scale, or a criterion concerning improvement after SD, we compared the individual scale or criterion with the mean of all scales/criteria. A mean of all scales/criteria is usually more reliable than a single variable and avoids extreme values. This strategy – defined by test theory – enables us to get the best estimation of the SD effect.

Differences between SAD patients and controls were calculated by Chi-Square and Fisher's Exact Test. Linear trends were calculated by regression analysis.

3. Results

Details of recruitment and the patient collective have been described in a previous paper (Brunner et

Table 1
Sleep deprivation response of SAD patients

| | Sleep deprivation response in the CR | | | | | | | | | | Relapse of the responders | | | | |
	GSI	DSI	DS 08:00	DS 20:00	VAS 11:00 ≥ 10 mm	VAS 20:00 ≥ 10 mm	VAS 11:00 > 0 mm	VAS 20:00 > 0 mm	Linear Comp.	Number of criteria	GSI	DSI	DS 08:00	VAS 11:00 ≥ 10 mm	VAS 11:00 > 0 mm
S 1.6	r[a]	r[a]	r	r	r	r	r	r	r	9/9 (100%)	•	•	rl	rl	rl
S 5.3	b	b	nr	r	nr	r	nr	r	nr	3/7 (43%)	•	•	–	–	–
S 7.1	r[a]	r[a]	nr	r	r	nr	r	nr	r	6/9 (67%)	rl	rl	–	rl	rl
S 8.1	r	r	r	r	nr	nr	r	r	r	7/9 (78%)	•	•	nrl	–	nrl
S 10.1	b	b	r	nr	r	nr	r	nr	nr	3/7 (43%)	•	•	rl	rl	rl
S 12.3	r	r	r	r	nr	r	r	r	nr	7/9 (78%)	nrl	nrl	nrl	–	nrl
S 13.1	nr	nr	nr	nr	nr	nr	nr	r	nr	1/9 (11%)	–	–	–	–	–
S 14.1	r	r	r	nr	r	nr	r	r	nr	6/9 (67%)	nrl	nrl	nrl	rl	rl
S 15.1	nr	nr	nr	nr	nr	r	nr	r	nr	2/9 (22%)	–	–	–	–	–
S 17.1	nr	r	nr	nr	r	nr	r	nr	nr	3/9 (33%)	–	rl	–	rl	rl
S 18.1	nr	nr	nr	nr	nr	r	nr	r	nr	2/9 (22%)	–	–	–	–	–
Σ	5r	6r	5r	5r	5r	5r	7r	8r	3r	49/95 (52%)	1rl	2rl	2rl	5rl	5rl
%	56	67	45	45	45	45	64	73	27	Mean	33	50	40	100	71

r = responder; nr = non-responder; [a] = HAM-D data; b = no HAM-D and CGI after SD; rl = relapse; nrl = non-relapse; – = non-responder; • = no data.

al., 1996). 11 SAD women (age range 27–66 y [mean±SD: 46.5±12.9 y]) and 8 control women (24–66 y; 50.4±12.5 y) completed the trial in winter.

3.1. SD-response in SAD (Table 1)

The highest rate of response, 8/11 (73%) was found when using a broad criterion of evening VAS rating improvement > 0 mm, or depression severity improvement (DSI 6/9, 67%). The lowest response rate of 3/11 (27%) was found when using the linear trends. If all 9 criteria were summed for each individual, the response rate averaged 52%.

After a night of recovery sleep the relapse rate of the responders depended on the criteria used: beween 100% (5/5; morning VAS rating worsening ≥ 10 mm) and 33% (1/3; GSI). The average relapse rate over all 9 criteria was 63%.

3.2. SD-effect in controls (Table 2)

The highest rate of mood improvement, 5/8 (63%), was found for the broad criterion of morning VAS rating improvement > 0 cm. The lowest rate of mood improvement, 1/8 (13%), was found for both morning and evening ratings of VAS improvement ≥ 10 mm. If all 7 criteria were summed for each individual, the rate of mood improvement averaged 29%.

For the controls, only the criteria of VAS > 0 mm

had sufficient subjects with mood improvement ($N = 5$) to measure relapse (all did so).

3.3. Comparison between SAD and controls

For each of the single criteria there was no significant difference between the response rate of the SAD patients and the improvement of mood of the controls (Chi-Square: morning DS rating $\chi^2 = .19$; evening DS rating: $\chi^2 = .01$; morning VAS ≥ 10 mm: $\chi^2 = 1.1$; evening VAS ≥ 10 mm: $\chi^2 = 1.1$; morning VAS > 0 mm: $\chi^2 = .2$; evening VAS > 0 mm: $\chi^2 = 2.5$; all Fisher's Exact Test n.s).

However, if we compare the 7 criteria common to both SAD and controls, patients reported an improvement of mood after SD more often than controls (Fisher's Exact Test, $P = .04$). Definition of the threshold for a positive judgement was that in a given subject, three or more of the 7 criteria must have shown mood improvement.

4. Discussion

The carefully controlled conditions of the constant routine permit very precise documentation of mood changes over time (for the detailed time course, see Fig. 3, Wirz-Justice, 1995). 52% of our SAD patients improved transiently with SD. This response rate is in the range (60%) reported in a survey of SD in major depression (Kuhs and Tölle, 1986; Wu and

Table 2
Improvement of mood after sleep deprivation of the controls

	DS 08:00	DS 20:00	VAS 11:00 ≥ 10 mm	VAS 20:00 ≥ 10 mm	VAS 11:00 > 0 mm	VAS 20:00 > 0 mm	Linear Comp.	Number of criteria
C 3.1	ni	i	i	i	i	i	i	6/7 (86%)
C 4.1	ni	i	ni	ni	ni	ni	ni	1/7 (14%)
C 5.1	i	ni	ni	ni	i	ni	ni	2/7 (29%)
C 6.1	ni	ni	ni	ni	i	i	ni	2/7 (29%)
C 7.1	ni	ni	ni	ni	i	ni	ni	1/7 (14%)
C 8.1	ni	ni	ni	ni	i	ni	i	2/7 (29%)
C 11.3	ni	ni	ni	ni	ni	ni	ni	0/7 (0%)
C 13.1	i	i	ni	ni	ni	ni	ni	2/7 (29%)
Σ	2i	3i	1i	1i	5i	2i	2i	16/56 (29%)
%	25	38	13	13	63	25	25	Mean

i = improvement; ni = no improvement or worsening.

Bunney, 1990). A critical metaanalysis of the SD response rate in relation to the year a study was carried out indicated a decline over time: from 69% in 1970–75 to 47% in 1986–90 (Elsenga, 1992). Even with this critical approach, the response rate found for SAD patients under constant routine conditions remains in the same range as found for non-seasonal major depression under normal clinical conditions.

The relapse rate of 63% is somewhat below the reported mean of 83% (Wu and Bunney, 1990). Although the number of patients is too small to make definitive comparisons, it is perhaps of interest to note that the relapse rate after light treatment is also lower in our SAD patient collective (Wirz-Justice et al., 1989, 1993, 1996) than found in the equivalent US studies (e.g. Rosenthal et al., 1984; Terman et al., 1989). For a discussion of this as yet not explicable difference, see Blehar and Lewy (1990).

In contrast, healthy controls did not improve markedly after SD (29% with mood improvement). Early studies reported little or no improvement of mood in healthy controls: 4/23 (17%; Pflug and Tölle, 1971) and 0/20 (0%; Gerner et al., 1979). Most healthy controls show a worsening of mood after SD and an improvement is rare. The small mood improvement in controls was reversed in all cases after recovery sleep. That we found no significant differences between SAD and controls using only a single criterion must be cautiously interpreted (Type II error possible).

If we take the mean improvement using all criteria (52%) as the most reliable and valid rating of a response to SD, we can say that 5 of these criteria provide a good estimate of SD response:

- improvement of global severity (in the GSI scale)
- depression self-rating scale in the morning and evening (DS/DS′)
- Visual Analogue Scale (VAS) in the morning and evening using the cut off improvement of ≥ 10 mm.

The linear trend analysis underestimates clinical response, whereas depression severity improvement (DSI) in the CGI scale and an improvement of any degree in the VAS overestimate the SD effect. Morning ratings are preferable for a good discrimina-tion, since diurnal variation with worse morning mood and evening improvement is often found to be a predictor of SD response (Reinink et al., 1990; Haug, 1996), and was indeed found in 6/11 SAD patients.

In summary, SAD patients showed a SD response rate similar to that reported for major depression without seasonality. Second, as rating scales discriminating SD response we propose the following: for the observer rating, the improvement of global severity (CGI) and as self-rating, the depression scale of von Zerssen and a simple 100 mm VAS using the criterion of ≥ 10 mm improvement in the morning.

Acknowledgements

References

Aitken, R.C.B., 1969. Measurement of feelings using visual analogue scales. Proc. R. Soc. Med. 62, 17–21.

American Psychiatric Association, 1987. Diagnostic and Statistic Manual of Mental Disorders (DSM-III-R), 3rd rev. ed. Washington, DC.

Blehar, M.C., Lewy, A.J., 1990. Seasonal mood disorders: consensus and controversy. Psychopharmacol. Bull. 26, 465–530.

Brunner, D.P., Kräuchi, K., Dijk, D.-J., Leonhardt, G., Haug, H.-J., Wirz-Justice, A., 1996. Sleep electroencephalogram in seasonal affective disorder and in control women: effects of midday light treatment and sleep deprivation. Biol. Psychiatry 40, 485–496.

Czeisler, C.A., Kronauer, R.E., Allan, J.S., Duffy, J.F., Jewett, M.E., Brown, E.N., Ronda, J.M., 1989. Bright light induction of strong (type 0) resetting of the human circadian pacemaker. Science 244, 1328–1333.

Elsenga, S., 1992. Sleep Deprivation and Depression. PhD thesis, Groningen.

Fähndrich, E., Linden, M., 1982. Reliability and validity of the Visual Analogue Scale (VAS). Pharmacopsychiatry 15, 90–94.

Gerner, R.H., Post, R.M., Gillin, J.C., Bunney, W.E., 1979. Biological and behavioral effects of one night's sleep deprivation in depressed patients and normals. J. Psychiatr. Res. 15, 21–40.

Hamilton, M., 1967. Development of a rating scale for primary depressive illness. Br. J. Soc. Clin. Psychol. 6, 278–296.

Haug, H.-J., Fähndrich, E., 1986. Problems in defining response in therapy studies. Pharmacopsychiatry 19, 170–171.

Haug, H.-J., 1996. Tagesschwankungen der Stimmung und therapeutischer Schlafentzug. In: Kaspar, S., Möller, H.-J. (Eds.), Therapeutischer Schlafentzug. Klinik und Wirkmechanismen. Springer, Wien, New York, pp. 165–171.

Kuhs, H., Tölle, R., 1986. Schlafentzug (Wachtherapie) als Antidepressivum. Fortschr. Neurol. Psychiatr. 54, 341–355.

Lam, R., Terman, M., Wirz-Justice, A., 1997. Light therapy for depressive disorders: indications and efficacy. In: Rush, J.A. (Ed.), Modern Problems in Pharmacopsychiatry: Clinical Decision Trees in the Pharmacotherapy of Mood Disorders. Karger, Basel, Switzerland, pp. 215–234.

Leibenluft, E., Wehr, T.A., 1992. Is sleep deprivation useful in the treatment of depression?. Am. J. Psychiatry 149, 159–168.

National Institute of Mental Health, 1976. 028 CGI. Clinical Global Impressions. In: Guy, W. (Ed.), ECDEU Assessment for Psychopharmacology. Rockville, MD, pp. 217–222.

Neumeister, A., Lucht, M., Kaspar, S., 1996. Kombination von Schlafentzug und Lichttherapie zur Behandlung depressiver Störungen. In: Kaspar, S., Möller, H.-J. (Eds.), Therapeutischer Schlafentzug. Klinik und Wirkmechanismen. Springer, Wien, New York, pp. 69–80.

Pflug, B., Tölle, R., 1971. Therapie endogener Depressionen durch Schlafentzug. Nervenarzt 42, 117–124.

Reinink, E., Bouhuys, A.L., Wirz-Justice, A., van den Hoofdakker, R.H., 1990. Prediction of the antidepressant response to total sleep deprivation by diurnal variation of mood. Psychiatry Res. 32, 113–123.

Rosenthal, N.E., Sack, D.A., Gillin, J.C., Lewy, A.J., Goodwin, F.K., Davenport, Y. et al., 1984. Seasonal affective disorder: a description of the syndrome and preliminary findings with light therapy. Arch. Gen. Psychiatry 41, 72–80.

Rudolf, G.A.E., 1996. Klinische Effekte des therapeutischen Schlafentzugs. In: Kaspar, S., Möller, H.-J. (Eds.), Therapeutischer Schlafentzug. Klinik und Wirkmechanismen. Springer, Wien, New York, pp. 19–32.

Terman, M., Terman, J., Quitkin, F., Stewart, J., McGrath, P., Nunez, et al., 1989. Dosing dimensions of light therapy: duration and time of day. In: Thompson, C., Silverstone, T. (Eds.), Seasonal Affective Disorder. CNS Clinical Neuroscience, London, pp. 187–204.

van den Burg, W., Bouhuys, A.L., van den Hoofdakker, R.H., Beersma, D.G.M., 1990. Sleep deprivation in bright and dim light: antidepressant effects on major depressive disorder. J. Affect. Disord. 19, 109–117.

von Zerssen, D., Koeller, D.M., 1976. Paranoid-Depressivitätsskala. Beltz Testgesellschaft, Weinheim.

Wehr, T.A., Rosenthal, N.E., Sack, D.A., Gillin, J.C., 1985. Antidepressant effects of sleep deprivation in bright and dim light. Acta Psychiatr. Scand. 72, 161–165.

Wirz-Justice, A., 1995. Biological rhythms in mood disorders. In: Bloom, F.E., Kupfer, D.J. (Eds.), Psychopharmacology. The Fourth Generation of Progress. Raven Press, New York, pp. 999–1017.

Wirz-Justice, A., Graw, P., Kräuchi, K., Gisin, B., Jochum, A., Arendt, J., et al. 1993. Light therapy in seasonal affective disorder is independent of time of day or circadian phase. Arch. Gen. Psychiatry 50, 929–937.

Wirz-Justice, A., Graw, P., Kräuchi, K., Pöldinger, W., 1989. Phototherapy in Switzerland: ''Mehr Licht''. In: Thompson, C., Silverstone, T. (Eds.), Seasonal Affective Disorder. CNS Clinical Neuroscience, London, pp. 169–185.

Wirz-Justice, A., Graw, P., Kräuchi, K., Sarrafzadeh, A., English, J., Arendt, J. et al., 1996. 'Natural' light treatment of seasonal affective disorder. J. Affect. Disord. 37, 109–120.

Wu, J.C., Bunney, W.E., 1990. The biological basis of an antidepressant response to sleep deprivation and relapse: review and hypothesis. Am J Psychiatry 147, 14–21.