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THE EFFECT OF SLEEP DEPRIVATION ON DEPRESSED PATIENTS

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In this paper an account is given of the effect of single-night sleep deprivation (SD) therapy in 124 depressive patients of different diagnostic groups. Phasic depressives showed a marked improvement after treatment by sleep deprivation. Because these improvements were often of short duration, we repeated the treatments and combined them with thymoleptic drugs. In the group of neurotic depressives the therapeutic effect of sleep deprivation varied; on the whole, however, the improvement was less marked. It is pointed out that the vital symptoms and "critical time" are of importance. Sleep deprivation can be explained as a resynchronization of disturbed circadian rhythms brought about by interrupting these rhythms.

Key words: Depression – sleep deprivation – circadian rhythms – therapy.

In view of the fact that sleep disturbance is one of the most common symptoms of depression and that many depressed patients complain of a longstanding sleeplessness, it would seem paradoxical to treat the patient by depriving him of a night's sleep.

However, *Schulte* (1966) described a female teacher who reported that when she was depressed the condition was easiest to bear after she had stayed awake all night. Since 1968, we have systematically investigated the effect of single-night sleep deprivation (SD), and we have given a report of the therapeutic effects of SD (*Pflug & Tölle* (1971)). Our results have been confirmed by other authors (*Kretschmar & Peters* (1973), *van den Burg & van den Hoofdakker* (1975), *Bhanji & Roy* (1975)). This paper gives an account of therapy by SD given to a larger number of patients.

MATERIAL AND METHODS

One hundred and twenty-four patients (45 men and 79 women) were examined. All the patients had marked depressive symptoms, and were divided into different nosologic-diagnostic groups. In all, 290 applications of sleep deprivation were observed. The patient groups, sex and age of the patients and the number of applications of SD are shown in Table 1.

Table 1. *Patient groups and number of applications of sleep deprivation*

Group	No. of patients			Average age (years)	No. of sleep deprivations
	Total	M	F		
I. Endogenous depression (unipolar)	45	16	29	43.9	127
II. Endogenous depression (bipolar)	12	6	6	42.0	39
III. Involutional depression	37	10	27	59.6	74
IV. Mixed phasic depression	8	3	5	45.2	14
V. Neurotic depression	22	10	12	36.7	36
Total	124	45	79		290

The patients were kept awake for a night under the observation of nursing staff. The morning before and the morning after depriving the patients of sleep and for the next few days the depressive symptoms were assessed on the rating scale devised by *Bojanovsky & Chloupkova* (1966). As well as providing a global depressive index, this scale takes 14 different symptoms into consideration. The evening before sleep deprivation we told the patients that they had to stay awake for the night. The night staff was given an assessment sheet to fill out for each patient describing the course of the night. The statistical methods used were primarily parametric, i.e., a t-test and analysis of variance in a simple randomizing A × B design, randomizing patients and treatments.

RESULTS

Table 2 shows the therapeutic effect of repeated applications of SD on the severity of the depression in the various diagnostic groups.

Table 2. *Therapeutic effect of sleep deprivation on the severity of depression.* (m = *average amount of reduction in the index of depression; n = number of applications of sleep deprivation.)*

	Endogenous depression (unipolar)		Endogenous depression (bipolar)		Involutional depression		Mixed phasic depression		Neurotic depression	
	n	m	n	m	n	m	n	m	n	m
First sleep deprivation	45	54.3	12	41.1	37	44.0				
Second sleep deprivation	29	35.5	8	52.1	18	31.1				
Third sleep deprivation	11	30.2	4	42.3	7	15.1				
Fourth sleep deprivation	9	27.1	4	33.0	3	22.0				
Further sleep deprivations	33	34.1	11	39.4	9	27.3				
Total	127	40.75	39	42.15	74	35.2	14	28.5	36	13.94

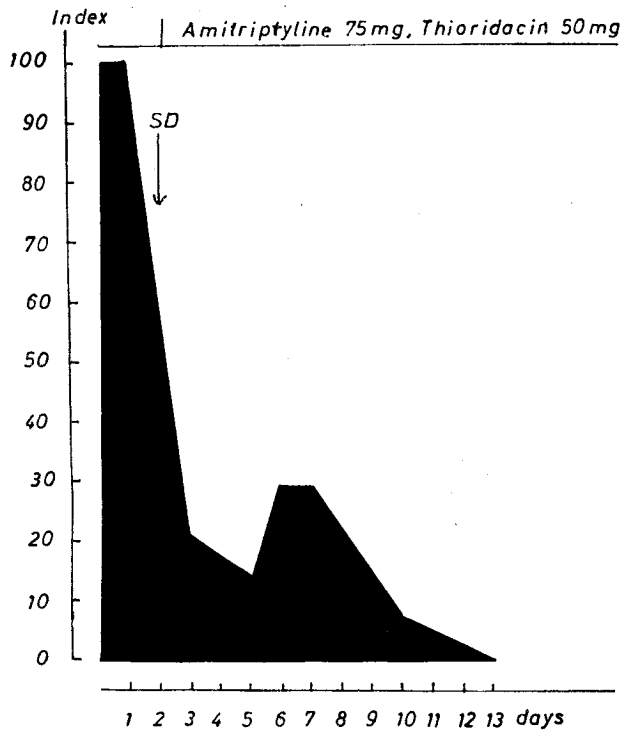

Fig. 1. *Example of marked improvement as measured on the index for reduction of depression in one patient. In 16 patients (35.6 %) one sleep deprivation (SD) was sufficient to alleviate the depression completely for a time.*

I. Endogenous depression (unipolar)

In the unipolar endogenous group (45 patients) in which the average age was 43.9 years there was an improvement on the day after SD in the main symptoms of depression: depressive mood, psychomotor phenomena and vegetative complaints. In some cases the improvement was very marked. In 16 of the patients (= 35.6 %) one SD was sufficient to alleviate the depression, causing it to disappear completely for the next few weeks. An example illustrating this is given in Fig. 1.

Fig. 1 shows the course of depression in a 29-year-old woman who had already been treated with thymoleptic agents without showing any signs of improvement. Having stopped all medication and observed the patient for 2 days during which there was no change in the clinical picture, we deprived her of sleep for one night. Until 4:30 she did not find it difficult to stay awake. Then there was a "critical time" during which she had to struggle against sleep. Following this "critical time" she said that she felt much better. On the day after SD, apart from a mild feeling of insecurity and uneasiness, she was free from depressive symptoms. From the night after SD on she did not have any sleep disturbances. A few days later there was a mild set-back for a brief period during which the patient felt less lively and mildly agitated. Thirteen days after SD all symptoms

had completely disappeared, and during the next 2 years we did not observe any further depressive episodes.

In the case of 29 patients (64.4 %) two or more treatments by SD were given, because the depression recurred 2 days after SD.

The course of depression in a 31-year-old female patient who was suffering from agitated depression and treated by repeated applications of SD is presented in Fig. 2. This patient also reported a critical time between 3 and 4 o'clock during all the nights of SD.

In five patients treatments by SD produced no change in the depressive symptoms. We observed that the effect was not as good if the patient fell asleep at all, even for a moment. One patient who fell asleep was worse after SD; later on more rigorous treatment by SD was therapeutically effective in this patient.

The profile of symptoms presented in Fig. 3 shows to what extent the various depressive symptoms are affected differently by SD.

It should be noted that depressive mood improved more than psychomotor retardation. This is important in that it reduces the danger of suicide and allows us to treat outpatients by SD (*Pflug* (1972), *Vass & Kind* (1974)). In the analysis

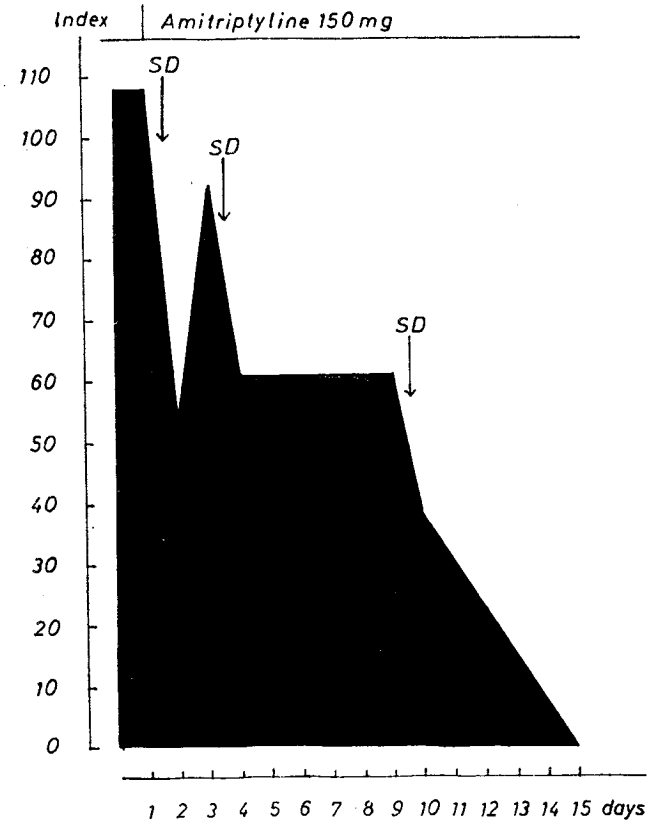

Fig. 2. *Course of depression in one patient suffering from agitated depression and treated by repeated applications of sleep deprivation (SD).*

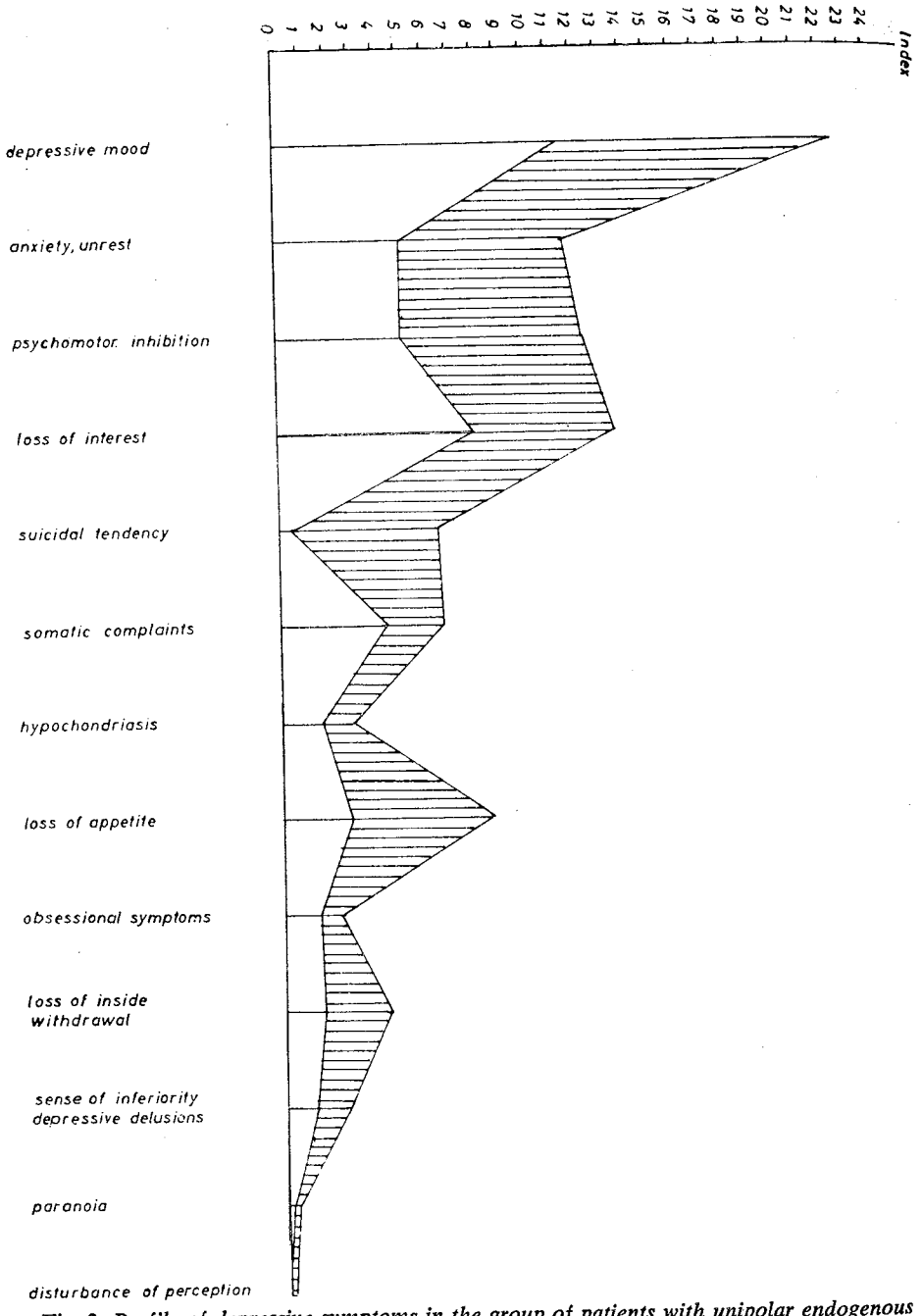

Fig. 3. *Profile of depressive symptoms in the group of patients with unipolar endogenous depression. The effect of sleep deprivation is shown, the shaded area indicating the degree of reduction in rating of each symptom.*

of variance, the fact that the various symptoms were influenced differently by SD was statistically significant.

II. Endogenous depression (bipolar)

In the bipolar endogenous depressive group (12 patients) in which the average age was 41 years the response to SD was similar to that of the unipolar group. We didn't observe any case in which a manic phase was definitely triggered off by SD, but this possibility cannot be excluded in one case.

III. Involutional depression

The involutional depressive group (37 patients) included all cases of unipolar endogenous depression whose first episode occurred after the age of 50. The average age of these patients was 59.6 years. The therapeutic effect observed in this group was in general less spectacular than in the two groups previously described.

Fig. 4 illustrates the course of treatment in a 61-year-old female patient who had been suffering from a depression with sleeplessness, loss of drive and withdrawal for 2 years at the time therapy began, a depression which had been brought about by a kidney operation and the stress of family quarrels.

Prolonged treatment with thymoleptics had induced no change and the patient had come a long way to our hospital to be treated by SD. Repeated therapy by SD at first without amitriptyline and later on with amitriptyline produced therapeutic results. In particular there was an impressive improvement in mood on the day after SD. After the fourth treatment, however, the patient showed no signs of improvement. On this occasion, no "critical time" was observed.

IV. Mixed phasic depression

The mixed group consisted of eight patients with recurrent depression. In five

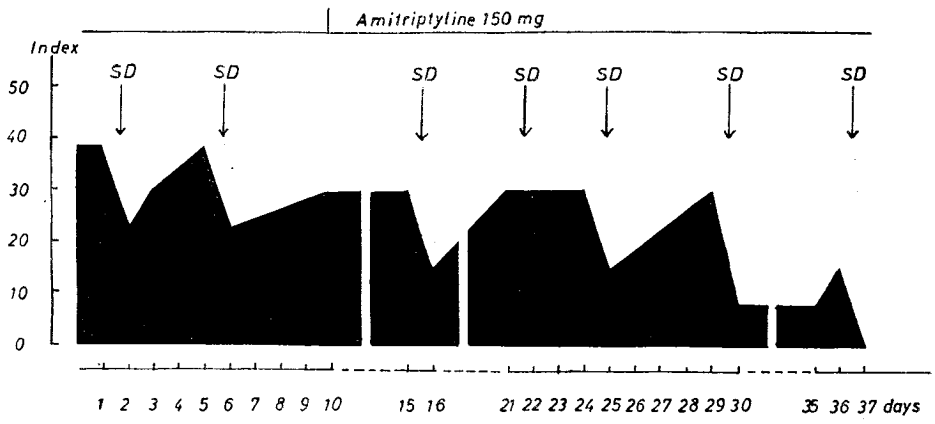

Fig. 4. *Course of depression in one patient with sleeplessness, loss of drive and withdrawal. Repeated treatment by sleep deprivation (SD) produced therapeutic results with a marked mood improvement the day after SD. After the fourth treatment, where no "critical time" was observed, there were no signs of improvement.*

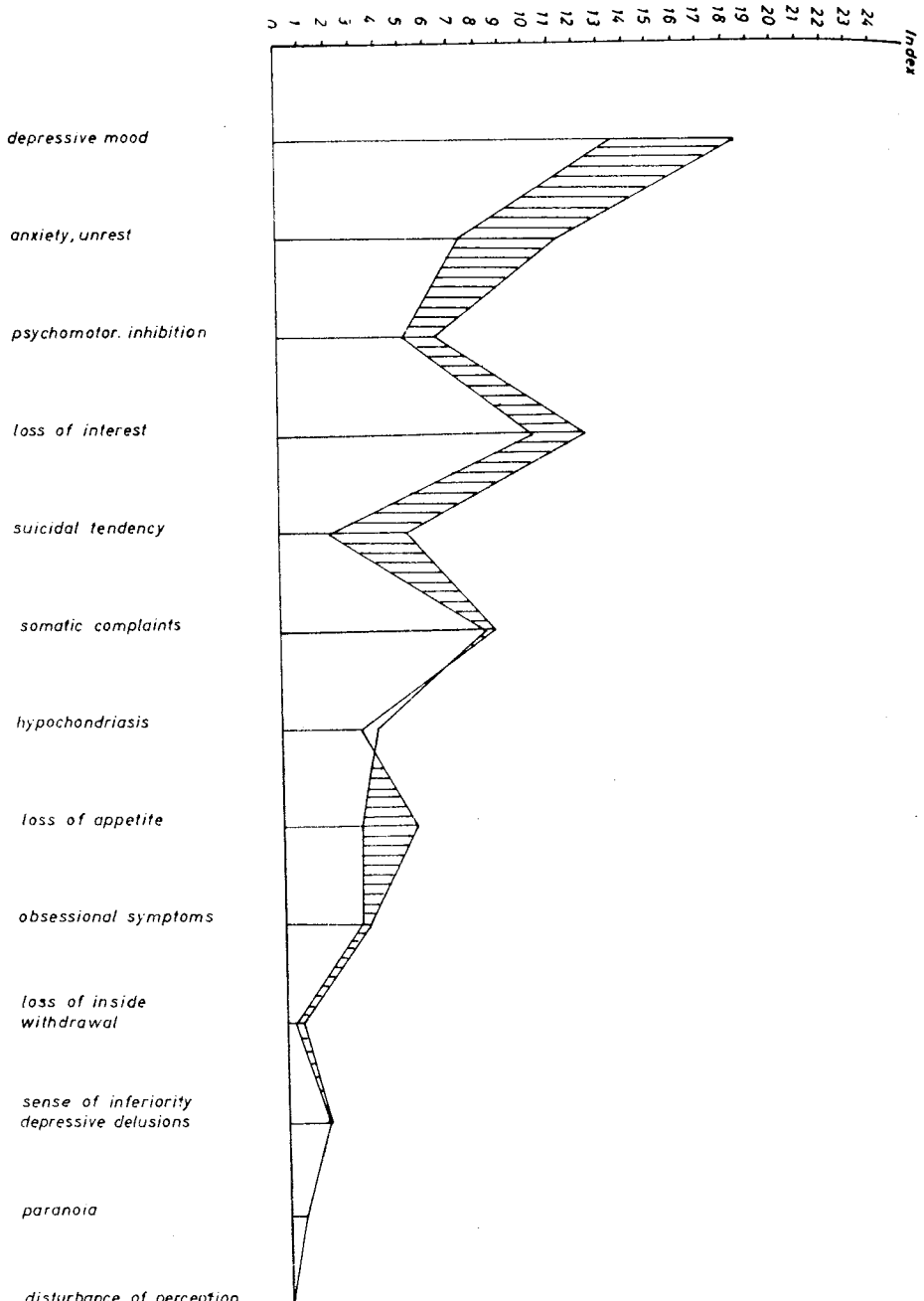

Fig. 5. *Profile of depressive symptoms in the group of patients with neurotic depression. The effect of sleep deprivation is shown, the shaded area indicating the degree of reduction in rating of each symptom, the unshaded area indicating an increase in rating.*

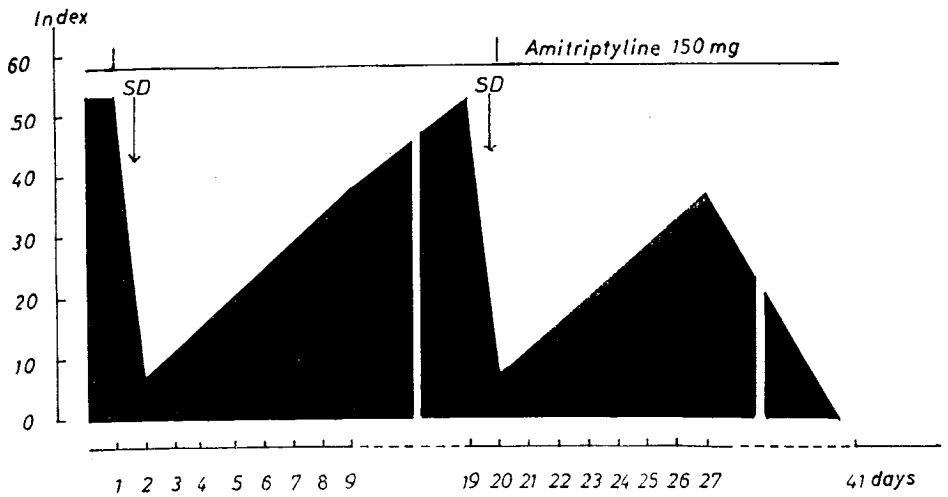

Fig. 6. *Course of depression in one patient treated with sleep deprivation (SD) alone and with sleep deprivation plus the thymoleptic, amitriptyline. Relapse during the days after SD can be prevented with the combination of SD and thymoleptic treatment.*

of these patients the clinical picture was coloured by schizophrenic symptoms (ideas of reference, hallucinations and paranoid delusions). The four patients with psychomotor inhibition improved; one patient with psychomotor agitation was considerably worse after SD. The patients with organic symptoms showed poor response to treatment or did not respond at all.

V. Neurotic depression

Results in the group of 22 patients with neurotic depression varied: 12 patients showed an improvement, six patients showed no change, and in four cases the patient was worse after treatment. On the whole, the response of patients in this group to SD was considerably poorer than that of the groups with endogenous depression. Fig. 5 illustrates the profile of symptoms of this group.

By dividing the patients into two groups, one with vital symptoms (somatic complaints, disturbed sleep, loss of appetite, diurnal variation) and one without any such symptoms, it is seen that the former respond significantly better to SD than the latter.

Overall response to sleep deprivation

In the case of recurrent depression there is a statistically significant correlation between response to SD and age in that the therapeutic effect decreases as the patient grows older. We found no relationship between response to SD and the sex of the patient. Neither did we find any significant correlation between the change in the severity of the depression induced by SD and the presence of diurnal variation.

Of the patients with endogenous depression, 53.9 % reported that during the night they were deprived of sleep, for a short time, generally between 4 and 6

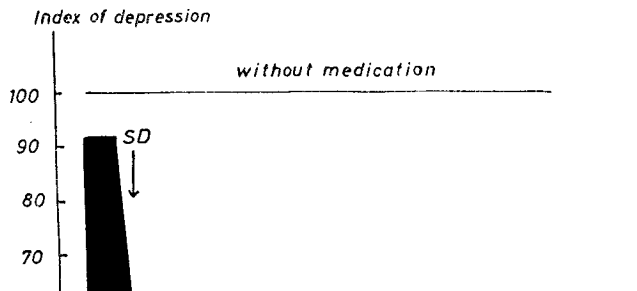

Fig. 7. *Course of depression in one patient representing the limited number of cases where treatment was managed with sleep deprivation (SD) without the supplementation of thymoleptic medication.*

o'clock, it was particularly difficult for them to stay awake. Very often there was a very sudden improvement after this "critical time". The groups of patients who experienced such a "critical time" responded significantly better to SD than the groups of patients who did not.

Comparison between patients who were given thymoleptics and those who were not given thymoleptics indicated that these agents had no bearing on the immediate effect of SD. They are, however, of value in the treatment regime. Our experience with a number of patients has led us to believe that relapse during the days after depression can be prevented by combining SD with thymoleptic treatment. This is illustrated in Fig. 6.

In a few cases we were able to manage without thymoleptics, as is shown in Fig. 7 in which the case of a 32-year-old man with endogenous depression is presented.

DISCUSSION

How can the effect of SD on depression which I have described be explained?

Various observations have revealed that there is a disturbance of the 24-hour rhythm during a depressive episode: e.g., the blood-levels of cortisol (*Sachar et al.* (1973)), of tyrosine (*Birkmayer & Linauer* (1970), *Klempel* (1972)) and the renin activity (*Breuer et al.* (1973)) show an alteration in the diurnal variation. The

same applies to the excretion of monoamine metabolites (*Riederer et al.* (1974)). Furthermore, the sleeping-waking rhythm is disturbed (*Mendels & Hawkins* (1971), *Zung et al.* (1964), *Hartmann* (1968)), the pattern of salivary secretion is changed (*Palmai & Blackwell* (1965)) and the patients themselves often experience a disturbance in their sense of time (*Edelstein* (1974)) and a marked diurnal variation in mood and drive (*Middelhoff* (1967)). The fact that these disturbances are of practical and of theoretical importance is shown by the results of interrupting the 24-hour rhythm in depressive patients by means of deprivation of REM-sleep (*Vogel et al.* (1973)) or of total SD for one night. From the results of research into circadian rhythms we can assume that a desynchronization of the various circadian processes occurs during a depressive episode. In the treatment of depression, SD acts as a method of manipulation which, like a "Zeitgeber", can bring about a resynchronization of desynchronized circadian rhythms and an entrainment to the 24-hour rhythm.

Investigations with animals (*Stroebel* (1969), *Richter* (1959)) and humans (*Jenner et al.* (1968)) indicate that during a depressive episode, periods of shorter or longer duration than 24 hours play an important part and that this disturbance in rhythm must be considered as a possible point of therapeutic attack by using, for instance, antidepressants, ECT and Li^+-salts. Investigations with plants and animals on the effect of Li^+-salts also point in this direction (*Engelmann* (1973)).

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