Psychiatr. Pol. 2015; 49(3): 423–433
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: http://dx.doi.org/10.12740/PP/30455

Sleep deprivation as a method of chronotherapy in the treatment of depression

Ewa Dopierała, Janusz Rybakowski

Department of Adult Psychiatry, Poznan University of Medical Sciences
Head: prof. dr hab. n. med. J. Rybakowski

Summary

Disturbances of circadian rhythms play an important role in the pathogenesis of affective illnesses, and their normalisation with methods of chronotherapy might become an important element of therapeutic treatment. Chronotherapy is based on a controlled exposure to environmental stimuli which affect biorhythms. One of the chronotherapeutic methods is sleep deprivation (SD). The article discusses the present status of SD in psychiatry, its methods and application in depression treatment. Presently the most recommended pattern is combining total sleep deprivation (TSD), sleep phase advance (SPA), pharmacotherapy, and sometimes also phototherapy. Such proceedings have proven short-term and long-term effectiveness, and they may also have beneficial effect in drug resistant depression. Among the therapeutic mechanisms of the sleep deprivation treatment, the following are influenced: catecholaminergic, serotonergic and glutamatergic neurotransmission, neurotrophic factors (mainly the brain-derived neurotrophic factor – BDNF), the immune system, the endocrine system, metabolism of some brain structures (mostly the prefrontal cortex) and gene expression related to biological clock. On the grounds of the efficiency, simplicity and safety of this method, authors think that SD in its modern version with SPA should be used more often as an element of depression treatment.

Key words: circadian rhythms, chronotherapy, sleep deprivation, depression treatment

Circadian rhythms and chronotherapy in affective disorders

The rotary motion of the Earth and, what follows it, the 24 hour light and darkness cycle results in recurring daily changes in animal behaviour and plant physiology which relate to the synchronization of growth, development, activity, sleep and nourishment.

The study was not sponsored

Circadian rhythmicity is explained by the existence of the internal biological clock, and its functioning aims to adapt the organism to changing environmental conditions.

Appropriate synchronization of basic biological rhythms is called the internal synchronization. Circadian rhythms (from Latin: circa – about, around, dies – day) in mammals are subcellularly controlled by a group of genes called "circadian clock genes". The internal cycle rhythm is slightly longer than the day, and its modulation down to 24 hours is under the influence of signals coming from the central nervous system (CNS) and sleep-wake rhythm shifts. This coordination is called the external synchronization.

In mammals, the main oscillator and the superior biological clock are suprachiasmatic nuclei (SCN) which are located in the hypothalamus. They generate circadian rhythms in the brain and whole body in the way that is synchronized with the solar cycle, due to the retino-hypothalamic tract (RTH) [1]. Melatonin – "the hormone of darkness" works in the opposite way. Night melatonin production by the pineal gland is controlled by SCN activity. Melatonin acts by its individual receptors in SCN, and similarly to the light, can cause shifts or synchronization of circadian rhythms [2].

The suprachiasmatic nuclei also regulate circadian noradrenergic activity (NA) of the locus coerulus (LC) which is located in the brainstem. Noradrenergic neurons of LC provide the regulation of the circadian sleep-wake cycle; maintaining the function of LC depends on light exposure. Deprivation of this exposure results in the loss of noradrenergic fibres [3]. Concentration of acetylcholine exhibits also circadian rhythmicity. Its amount within the cortex is higher during darkness [4]. The serotonergic tract, leading from the raphe nuclei and situated in the brainstem, provides stimulation of SCN independent of sun. Light-independent stimulating factors like physical activity, sleep or darkness, affect the activity of SCN much more weakly than light stimulation [5].

If signals needed for functioning of the main and peripheral oscillators are inappropriate, the homeostasis of the body is disturbed in the form of disorders of physiological processes dependent on circadian rhythm (i.a. melatonin and cortisol secretion). Examples of such desynchronization are the jet lag syndrome and depressive disorders [6]. Circadian rhythm disturbances are also characteristic of bipolar disorder (BD) and may be an important pathogenic factor. BD research shows that the polymorphism of the genes related to a circadian rhythm can affect the predisposition for this illness, its clinical course and treatment results [7]. In our research, we have shown the association between the polymorphism of some circadian clock genes and the effectiveness of the prophylactic treatment with lithium [8]. We have also observed the relation between those genes and temperamental dimensions connected with the predisposition for BD [9].

Chronotherapy is defined in psychiatry as a controlled exposition to environmental factors which affect biological rhythms and results in therapeutic effect in mental disorders [10]. Suggestions on the usefulness of chronotherapy can be already found in classic psychiatric texts. In 1794 Vincenzo Chiarugi advised increasing sunlight exposure in patients with depression, and avoiding light and noise exposure in agitated patients by putting them in dark rooms. In the second half of the XX century,

the antidepressant effects of sleep deprivation, sleep-wake cycle shift and bright light exposure were described, but the normothymic effect of prolonged bed rest and the antimanic effect of light exposure deprivation were described only in the last years [10]. Currently there are following chronotherapy methods: phototherapy (the bright light therapy – BLT; dawn and dusk simulation therapy), dark therapy (DT), sleep deprivation (SD), sleep phase advance (SPA) and integrated chronobiological therapies.

Sleep deprivation, methods and application

The first description of a mood improvement after a sleepless night was made by Pflug and Tolle in 1971 [11]. Since then SD has been used many times for experimental purposes to extend the knowledge about the pathophysiology of depression. After 30 years, Wu and Bunney [12] showed a meta-analysis of 1,700 people suffering from depression who were treated with SD and found that 50–60% of them showed a quick mood improvement after total sleep deprivation (TSD), whereof in 83% of the respondents, the effect disappeared after recovery sleep on following night.

Apart from a lot of observations about the results of TSD, research on selective REM sleep deprivation was carried out, based on the theory that the REM sleep is longer in patients with depression, and NREM sleep is shortened [13]. Throughout the 3 weeks, on every consecutive night, a gradual but more long-lasting effect was obtained in the half of the patients [14]. In other research, the second part of the night sleep deprivation where the REM sleep dominates was analyzed. The results were similar to these where TSD was applied. It shows that the antidepressant effect is connected to sleep deprivation in the second half of the night [6].

The minimal amount of sleep deprivation needed to obtain any antidepressant effect was not specified precisely but it has been shown that 2-hour sleep deprivation in the middle of the night gives a small clinical effect [15]. It is still not clear how many hours of sleep deprivation are needed to get a full antidepressant effect.

The typical SD therapy involves depriving of sleep for 36 hours, lasting from the morning of the first day to the evening of the next day (total sleep deprivation, TSD). While it lasts, naps are not allowed because they could worsen the effect. This kind of sleep deprivation is best documented because of its simplicity to carry out, fast results and no side effects [16]. Despite the similar percentage of progressions after partial sleep deprivation and TSD, the research which compared them directly showed that TSD is more effective that partial SD [15].

Certainly, the state of wake cannot last forever and SD ends with the first sleep episode. Referring to the earlier studies, one can expect worsening of a mood in the morning after waking up on the next day, even if a significant progress was seen before [12]. The depressive symptoms are usually less intense than before SD but on the next days, the effect wanes, and the intensification of symptoms comes back to the starting point before therapy [17].

To keep the antidepressant effect, therapies started using repeated sleep deprivation, which led to the typical fluctuation of symptoms between an improvement after SD and a deterioration of the mental state of the patients because of sleeping, with

a little benefit at the end. The trend towards improvement usually reversed within a few weeks after restoring the usual sleep-wake cycle [18].

Benedetti et al. [19] applied repeated TSD and the light therapy for one week in patients with bipolar disorder type 1. Those who achieved the antidepressant effect showed increased activity during the day and a forward shift of the sleep-wake rhythm compared to the period before the treatment. The patients without improvement did not show any circadian rhythm changes. Moving the sleep-wake rhythm forward seems to be correlated with an improvement after TSD and BLT in BD.

Researchers from Milan developed a protocol to describe the workflow in case of heavy depression without psychotic symptoms episode in the course of BD. A six-day pattern was suggested, including everyday morning 30-minute phototherapy and 3 nights with TSD alternating with nights when SPA is used. On the first day, TSD is used. On the next day, the patient starts an 8 hour sleep, 5 hours earlier than usually. On the third day, TSD is repeated, and on day four, the patient goes to sleep only 3 hours earlier. On the fifth day, TSD is repeated once again, and on day six, the patient starts to sleep an hour earlier than typically. Another recommended model of treatment is one-time TSD with 3 consequential nights with SPA (the time shift pattern as above – in turn: 5 hours, 3 hours and 1 hour ahead) and everyday morning phototherapy. Keeping the sleep-wake rhythm advance, appropriate hygiene of sleep, continuation of pharmacotherapy and BLT is advised after the applied procedure [6].

Sleep deprivation affects positively many depressive disorders regardless of aetiology and age. It also reduces negative symptoms of schizophrenia [20]. Women show to have a little worse SD effects than men [21]. In depression with psychotic symptoms, one needs to be very cautious because, despite better initial SD effects combined with clomipramine, a significant deterioration follows after the sleep episode, which is greater than with patients without psychotic symptoms [22], and intensification of psychotic symptoms may also occur [23]. In case of the mixed state, one should give up sleep deprivation because the normothymic and antimanic treatment is required. Even in BD patients with euthymia, a mania after SD may appear [24], which is particularly frequent in patients with rapid cycling bipolar affective disorder [25].

Sleep deprivation can cause an epileptic seizure, so history of epilepsy is a contraindication to the use of SD. Other side effects of sleep deprivation might be headaches and gastro-intestinal complaints [17]. The most often side effects of sleep deprivation are drowsiness and tiredness. Thus, patients, immediately after a period of SD, should not drive vehicles because of the increased risk of a road accident [10].

Recently Benedict et al. [26] proved that sleep deprivation increases hedonistic feelings in the context of eating food, regardless of glucose concentration in the plasma. In fMRI scanning, increased activity of the anterior cingulate cortex was indicated in patients who underwent SD in response to pictures showing food, compared to the control group.

The efficiency of sleep deprivation in depression treatment

Sleep deprivation shows similar efficacy in people with depression, independently from their pharmacologic treatment. The antidepressant effect of pharmacotherapy is faster when the treatment starts with SD. Deterioration after an episode of sleep occurs more rarely in pharmacologically treated patients, and the antidepressant effect of SD last longer then [6, 27]. Many studies have confirmed the acceleration and augmentation of the effect of antidepressant drugs (tricyclic as well as new generation drugs) through sleep deprivation. A lot of reports on effective combining pharmacotherapy with SD refer to the lithium therapy [6].

Riemann et al. [28], in 1999, described the effect of the sleep phase advance (SPA) and sleep phase delay (SPD) on prolonging of the therapeutic reaction after SD. SPA turned out to be more efficient than SPD. Prolonging of the SD antidepressant effect when combined with the bright light therapy (BLT) has also been proven [29].

In 2009, Wu et al. [30] presented results of an integrated antidepressant treatment where pharmacology, TSD, SPA and the bright light therapy were used. Depression symptoms were more reduced in people treated in an integrated way, compared to those treated pharmacologically only. The effect lasted for at least 7 weeks.

There are also reports on the efficacy of sleep deprivation in cases of drug resistant depression, combined with SPA and BLT. Benedetti et al. [31] described the short and long-term effect of repeated TSD combined with BLT in patients with drug-resistant depression in the course of bipolar affective disorder. Improvement criterion was reducing by half the score on the Hamilton Depression Rating Scale. Such effect was obtained in 44% of the drug resistant patients and 70% of the control group patients who were not resistant to antidepressant drugs. It turned out that the former resistance to pharmacotherapy correlates with the percentage of deterioration at a later time. After 9 months, symptomatic remission was retained by 57% of the non-drug resistant patients, where improvement was achieved by the means of chronotherapy, and only by 17% of the patients with improvement, who were formerly drug-resistant.

In 2013, Echizenya et al [32] applied TSD, combined with SPA, BLT and pharmacotherapy to 13 patients with treatment-resistant depression. All the people finished the study according to the procedure, and no significant side effects were observed. In 8 of the 13 patients, improvement (50% or bigger reduction of depression symptoms on HDRS) occurred on the sixth day of the study. One patient deteriorated on 13th day. In one patient, improvement was noted on 13th day. Four patients did not improve until 20th day of the study. Eventually, 8 of the examined patients (62%) held improvement until 20th day.

Combining BLT, lithium pharmacotherapy and three-time TSD can quickly lower suicidal tendencies and results in rapid improvement of mental state in BP drug-resistant depression. Recently, Benedetti et al. [33] examined 143 patients in this regard. One-hundred and forty-one people finished the study and 2 dropped off due to manic symptoms. 70% of patients (99 people) achieved 50% improvement on the HDRS in the first week, which was still present after one month in 55% (78 people). Suicidal tendencies declined both in patients who improved and in those without improvement.

Mechanisms of the therapeutic effect of sleep deprivation

The mechanism of sleep deprivation can be interpreted in the context of the pathogenic factors of depression, i.a. the monoaminergic neurotransmission, neuroplasticity, changes in the immune and endocrine systems, activity of brain structures as well as genes expression.

Sleep deprivation enhances noradrenergic [34] and dopaminergic neurotransmission [35]. Benedetti et al. [36] demonstrated a connection between the polymorphism of rs4680 catechol-O-methyltransferase (COMT) gene, an enzyme that inactivates noradrenaline and dopamine, and an antidepressant effect of SD and phototherapy. SD also stimulates serotonergic neurotransmission [37]. There is a association between the SD antidepressant effect and the polymorphism of the serotonin transporter gene (5-HTT-linked polymorphic region, 5-HTTLPR). Patients who are homozygous for the long version (allele 1) of 5-HTTLPR polymorphism show much better mood after TSD than those who are heterozygous or homozygous for the shorter variant [38].

There is also data indicating the effect of SD on the glutamatergic system. In a magnetic resonance spectroscopy study, Murck et al. [39] reported higher concentration of glutamate and glutamine in the dorsolateral prefrontal cortex, and Hefti et al. [40] proved an increased expression of mGluR5 glutamate receptor in the brain of healthy men after TSD. Given that the density of mGluR5 is reduced in patients with severe episode of depression, further study is justifiable, which would verify if the mechanism is involved in the antidepressant effect of sleep deprivation.

Sleep plays a significant role in the plasticity of the brain. It affects the regulation of many genes within the cortex and other brain structures. Glycogen synthase kinase 3β (GSK3 – β), besides of its role in neuroplasticity processes, plays an important role in the regulation of circadian rhythms. GSK3-β is inhibited by lithium and valproic acid, the two most important mood stabilizers. Benedetti et al. [41] demonstrated a relationship between the polymorphism of GSK3 – β gene and the antidepressant effect of TSD in depression in the course of BD. Gorgulu and Caliyurt [42] demonstrated an increase in the concentration of the brain-derived neurotrophic factor (BDNF) in patients treated with sleep deprivation, similar to antidepressant drugs and the electroconvulsive therapy. In healthy subjects, SD did not affect the level of BDNF. Taishi et al. [43] demonstrated that lack of sleep and a mild increase in temperature improve sleep and affect the expression of mRNA coding BDNF.

Sleep deprivation affects the immune system. The level of cytokines, both in patients with depression and healthy people, changes after SD, but it occurs in different ways. Sleep disorders in the course of depression may be responsible for an increased level of cytokines in the organism. SD, among others, causes an increase of concentration of interleukin 6 (IL-6). After an episode of sleep IL-6 returns to the initial level in patients with depression, and it remains raised in the control group. The amount of the antagonist of an interleukin-1 receptor (IL-1RA) is initially higher in depressed patients than in healthy subjects. In patients who achieved the effect after SD, the level of IL-1RA increased significantly during TSD, in contrast to patients without effect. During the sleep after deprivation, the level of IL-1RA increases in healthy individuals [44].

The level of thyroid hormones increases during sleep deprivation. It is the result of the stimulation of the hypothalamic-pituitary-thyroid axis. Also the sympathetic nervous system is activated by an anatomic connection to the thyroid gland [45]. In the course of SD, the concentration of cortisol increases considerably as a result of stimulation of the hypothalamic-pituitary-adrenal axis. During the first half of the day after SD, cortisol is above normal, particularly in patients with an antidepressant effect achieved, and then returns to normal. This rapid change of the cortisol concentration in serum coincides in time with the deterioration of mental state [46]. Schüssler et al. [47] describe the increase in the concentration of ACTH in blood serum after sleep deprivation and a small effect of SD on the level of ghrelin, which is an endogenous ligand for the growth hormone (GH) and affects the regulation of sleep and appetite.

Many neuroimaging studies have shown that the antidepressant effect of SD is related to certain metabolic and functional changes in the brain. People with a good SD effect had, before the deprivation, significantly higher metabolism within the orbital miedial prefrontal cortex and ventral anterior cingulate cortex compared to patients with no effect and to healthy ones. After sleep deprivation the activity of these areas normalized, the rate of glucose metabolism and blood flow was reduced [48], while within the dorsolateral prefrontal cortex, an increase was observed [49], which was correlated with clinical improvement. In patients with depression, there is a significant reduction in the activity of the dorsal nexus (DN), which is the dorsal medial prefrontal cortex. Sleep deprivation in healthy people reduces bilateral functional connectivity between posterior and anterior parts of the cingulate gyrus, but increases communication between DN and remote areas of the dorsolateral prefrontal cortex, which can be an important element of ongoing changes during antidepressant therapy [50].

Conti et al. [51], using an animal model, studied gene transcriptional changes caused by three effective methods of antidepressant treatment: the electroconvulsive therapy (ECT), SD and pharmacotherapy with fluoxetine (FLX), in seven different regions of the brain. The transcriptional changes proved to be specific for each of these methods. ECT and SD, giving fast antidepressant effect, induced changes in the transcription of genes relating to catecholamines. FLX treatment, which reduces symptoms of depression in a longer term, induced transcriptional changes within the serotonin system. In a similar way, ECT and SD influenced the same areas of the brain, particularly the locus coeruleus, whereas FLX caused changes mainly in the hypothalamus and raphe nucleus. ECT and SD, but not FLX, affected the transcription of genes which encode proteins involved in the synaptic plasticity of the hippocampus.

It is also suggested that the TSD antidepressant effect is connected to the resetting of malfunctioning "clock" genes, and a later episode of sleep may reactivate these irregularities. Bunney et al. [52] showed that in patients who achieved antidepressant effect after SD, the expression of the circadian clock genes (such as RORA, DEC2 and PER1) increases, but in patients without such effect, a significant decrease of their expression is found.

Recapitulation

Circadian rhythms disorders play an important role in the pathogenesis of affective disorders, and their normalization, by methods of chronotherapy, can be a significant element of treatment. One of the procedures in chronotherapy is sleep deprivation (SD), which is a minimally invasive method, has few contraindications and very rarely causes side effects. There are many benefits of using SD in the treatment of depression, including a rapid improvement. Currently, the most recommended procedure is combining total sleep deprivation (TSD) with sleep phase advance (SPA) and pharmacotherapy, or sometimes also bright light therapy (BLT). Such proceedings have proven short-term and long-term efficiency, and might positively affect drug-resistant depression. Because of the efficiency, simplicity and safety of this procedure, we think that, in its modern version with SPA, it should be used more often as an element of depression therapy. In dealing with patients who are resistant to pharmacotherapy, one should consider introducing SD and integrated chronobiologic treatment in such patients because it can shorten the duration of the treatment and effectively treat an episode of depression.

References

1. Hastings MH, Maywood ES, Reddy AB. *Two decades of circadian time*. J. Neuroendocrinol. 2008; 20(6): 812–819.
2. Arendt J. *Melatonin and human rhythms*. Chronobiol. Int. 2006; 23(1–2): 21–37.
3. Aston-Jones G, Chen S, Zhu Y, Oshinsky ML. *A neural circuit for circadian regulation of arousal*. Nat. Neurosci. 2001; 4: 732–738.
4. Gonzalez MM, Aston-Jones G. *Circadian regulation of arousal: role of the noradrenergic locus coeruleus system and light exposure*. Sleep 2006; 29: 1327–1336.
5. Challet E. *Minireview: Entrainment of the suprachiasmatic clockwork in diurnal and nocturnal mammals*. Endocrinology 2007; 148(12): 5648–5655.
6. Wirz-Justice A, Benedetti F, Terman M. *Chronotherapeutics for affective disorders. A clinician's manual for light and wake therapy*. Basel: Karger; 2013.
7. Gonzalez R. *The relationship between bipolar disorder and biological rhythms*. J. Clin. Psychiatry 2014; 75(4): 323–331.
8. Rybakowski JK, Dmitrzak-Węglarz M, Kliwicki S, Hauser J. *Polymorphism of circadian clock genes and prophylactic lithium response*. Bipolar Disord. 2014; 16: 151–158.
9. Rybakowski JK, Dmitrzak-Węglarz M, Dembińska-Krajewska D, Hauser J, Akiskal KK, Akiskal HS. *Polymorphism of circadian clock genes and temperamental dimensions of the TEMPS-A in bipolar disorder*. J. Affect. Disord. 2014; 159: 80–84.
10. Benedetti F, Barbini B, Colombo C, Smeraldi E. *Chronotherapeutics in a psychiatric ward*. Sleep Med. Rev. 2007; 11(6): 509–522.
11. Pflug B, Tőlle R. *Therapie endogener depressionen durch schlafentzug*. Nervenarzt 1971; 42: 117–124.

12. Wu JC, Bunney WE. *The biological basis of an antidepressant response to sleep deprivation and relapse: review and hypothesis*. Am. J. Psychiatry 1990; 147(1): 14–21.
13. Kupfer DJ, Foster FG, Reich L, Thompson SK, Weiss B. *EEG sleep changes as predictors in depression*. Am. J. Psychiatry 1976; 133(6): 622–626.
14. Vogel GW, Vogel F, McAbee RS, Thurmond AJ. *Improvement of depression by REM sleep deprivation, new findings and a theory*. Arch. Gen. Psychiatry 1980; 37: 247–253.
15. Giedke H, Wormstall H, Haffner HT. *Therapeutic sleep deprivation in depressives, restricted to the two nocturnal hours between 3:00 and 5:00*. Prog. Neuropsychopharmacol. Biol. Psychiatry 1990; 14: 37–47.
16. Gillin JC. *The sleep therapies of depression*. Prog. Neuropsychopharmacol. Biol. Psychiatry 1983; 7: 351–364.
17. Giedke H, Schwarzler F. *Therapeutic use of sleep deprivation in depression*. Sleep Med. Rev. 2002; 6: 361–377.
18. Benedetti F, Colombo C, Barbini B, Campori E, Smeraldi E. *Ongoing lithium treatment prevents relapse after total sleep deprivation*. J. Clin. Psychopharmacol. 1999; 19: 240–245.
19. Benedetti F, Dallaspezia S, Fulgosi MC, Barbini B, Colombo C, Smeraldi E. *Phase advance is an actimetric correlate of antidepressant response to sleep deprivation and light therapy in bipolar depression*. Chronobiol. Int. 2007; 24(5): 921–937.
20. Wirz-Justice A, Van den Hoofdakker RH. *Sleep deprivation in depression: what do we know, where do we go?* Biol. Psychiatry 1999; 46: 445–453.
21. Corsi-Cabrera M, Sánchez AI, del-Río-Portilla Y, Villanueva Y, Pérez-Garci E. *Effect of 38 h of total sleep deprivation on the waking EEG in women: sex differences*. Int. J. Psychophysiol. 2003; 50(3): 213–224.
22. Elsenga S, Van den Hoofdakker RH. *Response to total sleep deprivation and clomipramine in endogenous depression*. J. Psychiatr. Res. 1987; 21: 151–161.
23. Benedetti F, Zanardi R, Colombo C, Smeraldi E. *Worsening of delusional depression after sleep deprivation: case reports*. J. Psychiatr. Res. 1999; 33: 69–72.
24. Wehr TA, Sack DA, Norman E. *Sleep reduction as a final common pathway in the genesis of mania*. Am. J. Psychiatry 1987; 144: 201–204.
25. Wehr TA, Goodwin FK, Wirz-Justice A, Breitmaier J, Craig C. *48-hour sleep-wake cycles in manic-depressive illness: naturalistic observations and sleep deprivation experiments*. Arch. Gen. Psychiatry 1982; 39: 559–565.
26. Benedict C, Brooks SJ, O'Daly OG, Almèn MS, Morell A, Åberg K. et al. *Acute sleep deprivation enhances the brain's response to hedonic food stimuli: an fMRI study*. J. Clin. Endocrinol. Metab. 2012; 97(3): 443–447.
27. Leibenluft E, Wehr T. *Is sleep deprivation useful in the treatment of depression?* Am. J. Psychiatry 1992; 149: 159–168.
28. Riemann D, König A, Hohagen F, Kiemen A, Voderholzer U, Backhaus J. et al. *How to preserve the antidepressive effect of sleep deprivation: A comparison of sleep phase advance and sleep phase delay*. Eur. Arch. Psychiatry Clin. Neurosci. 1999; 249(5): 231–237.
29. Neumeister A, Goessler R, Lucht M, Kapitany T, Bamas C, Kasper S. *Bright light therapy stabilizes the antidepressant effect of partial sleep deprivation*. Biol. Psychiatry 1996; 39(1): 16–21.
30. Wu JC, Kelsoe JR, Schachat C, Bunney BG, DeModena A, Golshan S. et al. *Rapid and sustained antidepressant response with sleep deprivation and chronotherapy in bipolar disorder*. Biol. Psychiatry 2009; 66(3): 298–301.

31. Benedetti F, Barbini B, Fulgosi MC, Colombo C, Dallaspezia S, Pontiggia A. et al. *Combined total sleep deprivation and light therapy in the treatment of drug-resistant bipolar depression: acute response and long-term remission rates*. J. Clin. Psychiatry 2005; 66(12): 1535–1540.
32. Echizenya M, Suda H, Takeshima M, Inomata Y, Shimizu T. *Total sleep deprivation followed by sleep phase advance and bright light therapy in drug-resistant mood disorders*. J. Affect. Disord. 2013; 144(1–2): 28–33.
33. Benedetti F, Riccaboni R, Locatelli C, Poletti S, Dallaspezia S, Colombo C. *Rapid treatment response of suicidal symptoms to lithium, sleep deprivation, and light therapy (chronotherapeutics) in drug-resistant bipolar depression*. J. Clin. Psychiatry 2014; 75(2): 133–140.
34. Muller HU, Riemann D, Berger M, Muller WE. *The influence of total sleep deprivation on urinary excretion of catecholamine metabolites in major depression*. Acta Psychiatr. Scand. 1993; 88: 16–20.
35. Ebert D, Albert R, Hammon G, Strasser B, May A, Merz A. *Eye-blink rate and depression. Is the antidepressant effect of sleep deprivation mediated by the dopamine system?* Neuropsychopharmacology 1996; 15(4): 332–339.
36. Benedetti F, Barbini B, Bernasconi A, Fulgosi MC, Dallaspezia S, Gavinelli C. et al. *Acute antidepressant response to sleep deprivation combined with light therapy is influenced by the catechol-O-methyltransferase Val(108/158)Met polymorphism*. J. Affect. Disord. 2010; 121(1–2): 68–72.
37. Salomon RM, Delgado PL, Licinio J, Krystal JH, Heninger GR, Charney DS. *Effects of sleep deprivation on serotonin function in depression*. Biol. Psychiatry 1994; 36: 840–846.
38. Benedetti F, Serretti A, Colombo C, Campori E, Barbini B, di Bella D. et al. *Influence of a functional polymorphism within the promoter of the serotonin transporter gene on the effects of total sleep deprivation in bipolar depression*. Am. J. Psychiatry 1999; 156(9): 1450–1452.
39. Murck H, Schubert MI, Schmid D, Schüssler P, Steiger A, Auer DP. *The glutamatergic system and its relation to the clinical effect of therapeutic-sleep deprivation in depression – an MR spectroscopy study*. J. Psychiatr. Res. 2009; 43(3): 175–180.
40. Hefti K, Holst SC, Sovago J, Bachmann V, Buck A, Ametamey SM. et al. *Increased metabotropic glutamate receptor subtype 5 availability in human brain after one night without sleep*. Biol. Psychiatry 2013; 73(2): 161–168.
41. Benedetti F, Serretti A, Colombo C, Lorenzi C, Tubazio V, Smeraldi E. *A glycogen synthase kinase 3-beta promoter gene single nucleotide polymorphism is associated with age at onset and response to total sleep deprivation in bipolar depression*. Neurosci. Lett. 2004; 368(2): 123–126.
42. Gorgulu Y, Caliyurt O. *Rapid antidepressant effects of sleep deprivation therapy correlates with serum BDNF changes in major depression*. Brain Res. Bull. 2009; 80(3):158–162.
43. Taishi P, Sanchez C, Wang Y, Fang J, Harding JW, Krueger JM. *Conditions that affect sleep alter the expression of molecules associated with synaptic plasticity*. Am. J. Physiol. Regul. Integr. Comp. Physiol. 2001; 281(3): 839–845.
44. Voderholzer U, Fiebich BL, Dersch R, Feige B, Piosczyk H, Kopasz M. et al. *Effects of sleep deprivation on nocturnal cytokine concentrations in depressed patients and healthy control subjects*. J. Neuropsychiatry Clin. Neurosci. 2012; 24(3): 354–366.
45. Pereira JC Jr, Andersen ML. *The role of thyroid hormone in sleep deprivation*. Med. Hypotheses 2014; 82(3): 350–355.
46. Voderholzer U, Hohagen F, Klein T, Jungnickel J, Kirschbaum C, Berger M. et al. *Impact of sleep deprivation and subsequent recovery sleep on cortisol in unmedicated depressed patients*. Am. J. Psychiatry 2004; 161(8): 1404–1410.

47. Schüssler P, Uhr M, Ising M, Weikel JC, Schmid DA, Held K. et al. *Nocturnal ghrelin, ACTH, GH and cortisol secretion after sleep deprivation in humans*. Psychoneuroendocrinology 2006; 31(8): 915–923.
48. Wu J, Buchsbaum MS, Gillin JC, Tang C, Cadwell S, Wiegand M. et al. *Prediction of antidepressant effects of sleep deprivation by metabolic rates in the ventral anterior cingulate and medial prefrontal cortex*. Am. J. Psychiatry 1999; 156(8): 1149–1158.
49. Wu JC, Gillin JC, Buchsbaum MS, Schachat C, Darnall LA, Keator DB. et al. *Sleep deprivation PET correlations of Hamilton symptom improvement ratings with changes in relative glucose metabolism in patients with depression*. J. Affect. Disord. 2008; 107(1–3): 181–186.
50. Bosch OG, Rihm JS, Scheidegger M, Landolt HP, Stämpfli P, Brakowski J. et al. *Sleep deprivation increases dorsal nexus connectivity to the dorsolateral prefrontal cortex in human*s. Proc. Natl. Acad. Sci. U. S. A. 2013; 110(48): 19597–19602.
51. Conti B, Maier R, Barr AM, Morale MC, Lu X, Sanna PP. et al. *Region-specific transcriptional changes following the three antidepressant treatments electro convulsive therapy, sleep deprivation and fluoxetine*. Mol. Psychiatry 2007; 12(2): 167–189.
52. Bunney BG, Bunney WE. *Mechanisms of rapid antidepressant effects of sleep deprivation therapy: clock genes and circadian rhythms*. Biol. Psychiatry 2013; 73(12): 1164–1171.

Address: Ewa Dopierała
Department of Adult Psychiatry
Poznan University of Medical Sciences
60-572 Poznań, Szpitalna Street 27/33