Light therapy in patients with depression and insomnia in Department of Psychiatry 363 in Gothenburg

Master thesis in Medicine

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Abstract

Introduction

Depression and different anxiety disorders belong to the most common public health problems in the world today. At least 25 % of all woman and 15 % of all men will at least once during their lifetime seek treatment for a depressive episode. The treatment alternatives are many and vary depending on the severity and precipitating circumstances; everything from consolidating interview, psychotherapy, anti-depressive medicines to electro-convulsive therapy. Several of them are very effective, however, not all patients respond to antidepressants and there may be considerable side effects.

A relatively recent form of treatment is chronobiology, where the organic circadian rhythm is pre-dominantly manipulated to treat mental symptoms. Previous studies have shown results suggesting that bright light therapy could be an adjuvant treatment to other antidepressants, not only in seasonal affective disorder but also in major depression. The Swedish National Board of Health and Welfare (Socialstyrelsen), however, has called for more evidence from scientific research before recommending light therapy.

Aim

The aim of this thesis was to evaluate the role of the most common chronobiological method, bright light therapy, as adjuvant treatment in patients with affective disorder and contribute to the knowledge of light therapy and its possible impact on depression, insomnia and medication needed.

Methods

Bright light therapy was introduced as an adjuvant therapy and offered to suitable patients admitted to Department 363 Sahlgrenska University Hospital/Östra in October 2013. Patient records were collected prospectively for those receiving bright light therapy as adjunctive treatment and retrospectively for historical controls. The first 18 consecutive patients who completed the adjuvant bright light therapy were included. For

each of the 18 patients two patients admitted up to three years previously were included as controls. The controls had to: a) be same sex, b) be at a similar age at admission (within one to two years) and c) meet the criteria for bright light therapy without it being available.

The patient records included results from the two questionnaires: The Insomnia Severity Index (ISI) and the self-rating version of Montgomery–Åsberg Depression Rating Scale (MADRS-S). ISI is a diagnostic questionnaire used to evaluate the severity of insomnia and MADRS-S is a diagnostic questionnaire used to evaluate the severity of depressive disorders in affective patients.

Results

The mean age in the bright light therapy group was 39.1 years compared to 38.8 in the control group and in each group there were more woman, 72 %. The mean length of stay was 16 days for the light therapy group and 19 for the control group - a 3-day shorter stay for the those who had received bright light therapy. The mean MADRSs end score was 27 points for the light therapy group and 23 for the control group - a 4-point higher score for the patients who had received light therapy. The total accumulated dose of diazepam equivalent of benzodiazepine for the whole hospital stay for the control group was 100 mg and 75 for the light therapy group. Patients did not experience severe side effects and no patient switched to a manic state. The daily average dosage was 4.8 respectively 4.3 mg/day. However, these results did not reach statistical significance.

Discussion and conclusion

This study did not find a significantly more rapid improvement in depressive self-scoring and insomnia which might be due to too small groups. Though, it provides support to continue studying light therapy in patients with affective disorder as the results point in the direction that light therapy possibly could shorten the length of stay and reduce the consumption of diazepam Also there were few to no side effects and light therapy could be a valuable alternative for hard-to-treat patients. A randomized controlled trial with a higher number of patients would be necessary for achieving high statistical power. It

would also be interesting if such a study looked further into the use of benzodiazepines and if it would be possible to decrease the use of these highly dependence producing medications with light therapy.

Introduction

Depression and insomnia

According to the Swedish National Board of Health and Welfare (Socialstyrelsen - a Swedish government agency) depression and different anxiety disorders belong to the most common public health problems in the world today. In Sweden at least 25 % of all woman and 15 % of all men will at least once during their lifetime seek treatment for a depressive episode. These numbers differ from different studies and depending on how you classify different affective disorders [1].

Sleep problems are a common symptom of various psychiatric disorders and particularly in depression. A majority of depressed patients (about two thirds) suffer from insomnia or other sleep problems [2]. Sleep problems increase the risk of developing suicidal tendencies and poorer treatment outcome and should accordingly be counted as a core symptom of depression [3], [4].

Biological rhythms in psychiatry

Observations have been made showing that some affective disorders show periodicity associated with various factors, such as winter depression with the seasons, and also for patient with rapid cycling bipolar disorder [5]. During a depression the diurnal cycle of cortisol gets arrhythmic and the cortisol levels get higher, reflecting an internal desychronization [6]. There is well-documented research on circadian fluctuation in depressed patients' mood and behavior, which can be related to neuroendocrine and physiological changes in the brain [7]. This may be seen as evidence that depression reflects an internal desynchronization of endogenous chemicals and hormones in the brain [8].

Biological mechanism of circadian timing

The main control of the circadian system in the brain and body is the so-called biological clock, located in the hypothalamus (the SCN, the suprachiasmatic nucleus) that drives the circadian rhythms and makes our biological day slightly longer than 24 hours [9]. The SCN is synchronized to the light cycle via retinal input. Light has decisive effect in

human circadian rhythm and this effect appears to be stronger than the social effects. Studies show that even though light is not the only input that controls the circadian rhythms, it is probably the most powerful input, more powerful than social input [10] or even darkness and sleep [11].

Controlled by the SCN, the hormone melatonin is produced in the corpus pineale. Retinal light inhibits the synthesis of melatonin. Meanwhile, melatonin has a blocking effect on melatonin receptors in the SCN [12]. If administrated as a pill, melatonin can be given to induce sleep and synchronize the circadian rhythm [13]. The timing of light or melatonin intake is important in the regulation of the circadian rhythm and biological clock. Morning light or evening administrated melatonin shifts the biological clock earlier, and, whereas evening light or morning administrated melatonin shift the biological clock later [14], [15], [16].

Non-light-dependent neurochemical input to the SCN comes from the nucleus raphe (serotonergic enervation). Social factors, such as working schedules and daily routines, activates directly or indirectly the SCN, since they determine the timing of food intake, bedtime, physical labor and so on [17]. The SCN also gets input from the parts of the brain that controls sleep regulation. In addition to the brain's primary biological clock, we have circadian oscillators in all the body’s organs and cells, so-called peripheral clocks [18]. The homeostatic sleep pressure interacts with the circadian pacemaker depending on the timing and structure of sleep. According to this model, deregulation of both processes lead to depression and their interaction may explain mood fluctuations during the day [19].

Treatment alternatives

The treatment alternatives are many when it comes to depression. Several of them are very effective, but not all patients respond to antidepressants or tolerate all the medicines. Also there is the problem with the slow onset of action, which makes it necessary for some patients to stay a long time at hospital in order to be monitored until the antidepressants show effect. Electroconvulsive treatment is fast but has several

disadvantages, such as necessary anesthesia and side effects. This indicates that more options with fast onset and few side effects that could be combined to different treatments are needed. Studies show that light therapy is effective in different types of depression and is a good alternative as an adjuvant to the normal treatment [20].

Most antidepressant medications affect sleep pattern. Some antidepressants may have an activating effect; others may have sedative effects by affecting either histamine receptors or sigma receptors [21]. Several studies show that combined antidepressant and hypnotic medication lead to better results and faster improvements [22]. Melatonin agonists (such as agomelatine) seem to have both antidepressant and sedative effect by advancing the circadian phase [23].

Normally, hypnotics are prescribed to patients with insomnia regardless of underlying diagnosis. There are several medications without documented addictive effects (alimemazin, prometiazin, hydroxizin), but there is not clear evidence that they affect sleep patterns negatively. However, they do have long half-life and can cause unpleasant side effect such as daytime sleepiness. Benzodiazepine hypnotics and hypnotics with similar pharmacological profiles have a more selective sleep effect, but their long-term effect is more questionable. This type of medication affects the sleep pattern from long-term use, although the tolerant-generating effects are overestimated [24].

What is chronobiological therapy?

Bright light therapy arises from chronobiological therapy which is defined as the "controlled exposure to environmental stimuli that act on the biological rhythms" to achieve therapeutic efficacy of certain psychiatric disorders [25], [26].

Light therapy

The psychiatrist and scientist Norman E. Rosenthal was the first to describe seasonal affective disorder and as treatment tried to mimic a summer day through light therapy in the early 1980s [27]. Ever since 1984 when Rosenthal reported on the first clinical trial of light therapy this field of science has developed tremendously [28]. It has now been shown in repeated studies that it is not necessary to mimic a whole summer day, 30

minutes is sufficient [29], [30]. There is reasonable evidence that light therapy is significantly more effective than placebo in patients with depression [31]. A double blinded, placebo controlled study where light therapy was used as an adjuvant to SSRI treatment showed more rapid (within a week) and more profound (more than 30 %) improvements in the light therapy group compared to the control group [32], [33]. Light therapy according to current protocol is a safe method with few side effects [34] that can synchronize circadian rhythms and also has energizing effect even in healthy individuals [35].

Why more research on light therapy?

Even though several studies indicate that light therapy has a positive effect on patients with depression the Swedish National Board of Health and Welfare (Socialstyrelsen) do not recommend light therapy with this indication. Socialstyrelsen has reviewed several articles on light therapy. However, all these do not follow the same protocols with a light box with a 10.000 lux capacity which the studies indicating that light therapy has good effect are based on. Also, Socialstyrelsen's national guidelines on the subject were summarized in 2009 and are not completely up to date. In these guidelines they do not consider these studies sufficient to draw the conclusion that light therapy is a good compliment to medical treatment. However, they do recommend that light therapy should be conducted in departments as part of scientific research in the area [1].

Aim

The aim was to evaluate bright light therapy as treatment adjuvant in admitted psychiatric patients with affective disorder. Specific outcomes studied were: self-rated depressive symptoms, self-rated insomnia and medication needed.

The hypothesis was that light therapy could lead to faster response in depression, shorten length of hospital stay and improve sleep in patients with affective disorder. The question I wanted to answer was twofold: Can light therapy lead to faster response in depression in affective patients and improve their sleep? And: Does light therapy as adjunct to regular treatment reduce the usage of benzodiazepines?

Material and methods

Study design

Bright light therapy was introduced as an adjuvant therapy offered to suitable patients admitted to Department 363 Sahlgrenska University Hospital/Östra in October 2013. Patient records were collected prospectively for the first 20 consecutive patients that had been treated with light therapy. Of these, 18 patients completed the light therapy treatment and were included in the light therapy group. One patient did not consider that she was in need of psychiatric care and wanted to go back to school and left the department prematurely. The second patient did not complete her light treatment because she did not enjoy the circumstances of the light treatment (having to get up early in the morning) but stayed at the hospital and continued her psychiatric medical treatment.

To achieve a control group a list of all patients admitted to Department 363 from 1 January 2010 to 30 September 2013 was requested with patients diagnosed with any of the following ICD-10 was used:

F31.3 – Bipolar affective disorder, current episode mild or moderate depression
F31.4 – Bipolar affective disorder, current episode severe depression without psychotic symptoms
F31.8 – Other bipolar affective disorders
F31.9 – Bipolar affective disorder, unspecified
F32.0 – Mild depressive episode
F32.1 – Moderate depressive episode
F32.2 – Severe depressive episode without psychotic symptoms
F32.8 – Other depressive episodes
F32.9 – Depressive episode, unspecified
F33.0 – Recurrent depressive disorder, current episode mild
F33.1 – Recurrent depressive disorder, current episode moderate
F33.2 – Recurrent depressive disorder, current episode severe without psychotic symptoms
F33.4 – Recurrent depressive disorder, currently in remission
F33.8 – Other recurrent depressive disorders
F33.9 – Recurrent depressive disorder, unspecified

For each of the 18 patients who recieved ligh therapy, two patients were included as controls who had to: a) be same sex b) be at a similar age at admission (within one to two years) and c) meet the criteria for bright light therapy without it being available.

This resulted in a control group of 36 patients. In total 95 patients were examined from the list of possible patients for the control group, and 59 patients were not considered suitable for light therapy since they did not meet the criteria below or chose to discontinue their treatment prematurely.

Even though the different data variables were supposed to be registered in the patient records according to the department routine this was not the always the case. Because of this all data for all variables could not be retrieved. The numbers of patients with available data are given in all tables.

Criteria for light therapy

The patient had to suffer from an affective disorder, including both unipolar and bipolar affective disorder, and insomnia. This affective episode could not be manic, hypomanic or rapid cycling. The patient had to be able to make his/her own informed decision whether to receive light therapy. The patient had to be over 18 but not be 70 years or older since these patients were supposed to be cared for in the psychiatric care for the elderly. The patient could not suffer from an ongoing psychosis and could not be treated for substance abuse or have withdrawal symptoms. The patient could not be acutely suicidal or treated under involuntary commitment (with support of Lagen om psykiatrisk tvångsvård, the Swedish Compulsory mental care act). The patient cannot undergo electroconvulsive therapy and receive light therapy.

Other exclusion criteria were: epilepsy, age-related macular degeneration, retinal changes or other fundus diseases, porphyria, systemic lupus erythematosus, chronic actinic keratosis or solar urticaria, The patient could not use medication that can cause photosensitivity of the skin and eyes such as certain antipsychotics, psoralen, anti-arrhythmic (amiodarone), antimalarial drugs, medicine for rheumatism, porphyrin or St. John's wort.

Material

Philips EnergyLight HF3319/01 was selected as light source for the bright light therapy. Since there are no official agency regulating light boxes for light therapy, the light box was chosen in accordance with the clinical manual for light therapy Chronotherapeutics for affect disorders [36] that suggests that the lamp model should have been successfully used in peer-reviewed clinical trials, have sufficient ultraviolet screening and provide soft broad-band white light up to 10.000 lux of illumination at a comfortable distance for the patient. The Philips EnergyLight HF3319/01 meet these criteria and has meets the criteria for safety regarding UV screening according to the European Declaration of Conformity.

Treatment

Since it is not practical to measure melatonin in blood an estimation of the melatonin levels can be made using the self-assessment questionnaire Morningness-Eveningness Questionnaire (MEQ), which has shown good correlations between melatonin levels and different chronotypes in individuals [37]. To determine which time to start light therapy was most suitable the MEQ questionnaire was used. Since this questionnaire is not yet translated into Swedish, an English version was handed out to each patient to receive light therapy and, if needed, translated by the nursing staff to the patient. The treatment was given for 30 minutes each morning, at a predetermined time, at a sitting distance of 15-20 centimeters. The patient was allowed to read a book, use his/her smart phone, eat breakfast or do other activities as long as the patient did not cover his/her eyes. The patient was also allowed to take smaller breaks to use the bathroom as long as the treatment continued within a few minutes.

Data

All clinical records from January 2010 were predefined to contain demographics. The demographics always registered were age, gender, employment status, home-ownership and relationship status.

In the same way the patient records included results from the two questionnaires: the Insomnia Severity Index (ISI) and the self-rating version of Montgomery–Åsberg Depression Rating Scale (MADRS-S). ISI is a diagnostic questionnaire used to evaluate

the severity of insomnia. The score ranges from 0-28, where 28 is the most severe (see appendix). MADRS-S is a diagnostic questionnaire used to evaluate the severity of depressive disorders in affective patients. The score ranges from 0-60, where 60 is the most severe (see appendix). Both questionnaires are used as a routine in the department to monitor insomnia and depression from the day the patient is admitted to the psychiatric ward, and then weekly till the day the patient is discharge from the hospital. At the time for discharge the nursing staff has been informed to hand out these questionnaires one last time.

Furthermore, psychiatric and somatic medication for each day of the hospital stay was collected. The psychiatric medication has been divided into five groups, based on the purpose of the medication: antidepressants, antipsychotics, mood stabilizers, hypnotics and sedatives. To convert benzodiazepines to diazepam the memorandum for equivalent doses of benzodiazepines used in Västra Götaland, Sweden was used (see appendix).

Data analysis and statistical methods

All data has been depersonalized and collected into an excel sheet. All statistical analyses were made using IBM SPSS statistics 22.0.0. (SPSS Inc, Chicago, IL, USA). To determine if the different sets of data from the two groups are significantly different from each other, a t-test has been used for each analysis. User defined missing values are treated as missing. Statistics for each analysis are based on the cases with no missing or out-of-range data for any variable in the analysis.

Ethics

As this study is considered to be a quality control study, this study did not need to be approved by the Ethics committee according to the Swedish legislation.

Since light therapy is a non-invasive, well defined and considered to be one of the safest treatments in psychiatric care, with negligible short-term side effect and no known long-term side effects, that has been studied and implemented in treatment routines in hospitals all over the world [35], no special ethical considerations were required.

Results

These are the results for the first consecutive 18 patients from 1 October 2013 who has fulfilled their light therapy treatment at Department 363 Sahlgrenska University Hospital/Östra and the control group of 36 patients with same sex and closest possible similar age fulfilling the criteria of light therapy, identified from a list of all patients from 1 January 2010 to 30 September 2013, diagnosed with an affective disorder.

Demographics

Demographic variables of the light therapy group and the control group are displayed in table I. The mean age was 39.06 years for the light therapy group and 38.81 for the control group, and 72 % were females and 28 % males in both groups. Patients living with a partner was 28 % for the light therapy group and 22 % for the control group and all patients in the light therapy group (100 %) were currently living in their own home and were not living in a homeless shelter, institution, temporary housing or other facility compared to 78 % in the control group. The percentage of patients being employed, studying or receiving retirement pension due to age (not because of illness) was 39 % for the light therapy group and 58 % for the control group.

Table I – Demographics of patients and controls

Variable	Light therapy n=18	Controls n=36
Age	39.1±15.9	38.8±16.5
Female gender	72 %	72 %
Living with partner	28 %	22 %
Employed or student	39 %	58 %
Living in own home	100 %	78 %

Hospital stay

The length of stay for the light therapy group and the control group are displayed in table II. The mean length of stay was 16.2 days for the light therapy group and 19.1 for the control group. This makes a difference of 2.9 days, or 15 % shorter hospital visit for the patients who had received the light therapy treatment. These results are not statistically significant.

Table II – Main outcome of patients and control

Variable	Light therapy n=18	Controls n=36
Hospital stay	16.2±7.0	19.11±8.2
MADRS end score	27.5±13.7[a]	23.2±11.3[b]
ISI end score	13.0±7.6[a]	13.2±7.3[b]

a) n=17, b) n=28

Montgomery-Åsberg Depression Rating Scale

The MADRS-s end score for the light therapy group and the control group are displayed in table II. All of the 18 patients in the light therapy group, and 28 out of 36 in the control group self-rated themselves, before leaving the department. The mean MADRS-S end score was 27.5 points for the light therapy group and 23.2 for the control group. This makes a difference of 4.3 points, or 18 % higher score for the patients who had received the light therapy treatment.

Table III shows the first and MADRS-S scores of the hospital stay. The mean 1st MADRS-S score was 32.22 for the light therapy group and 33.81 for the control group. This means that the light therapy group improved 4.75 points or 15 % during their stay, whereas the control group improved 10.6 points or 31 %. These results are not statistically significant.

Table III – MADRS-s and ISI scores

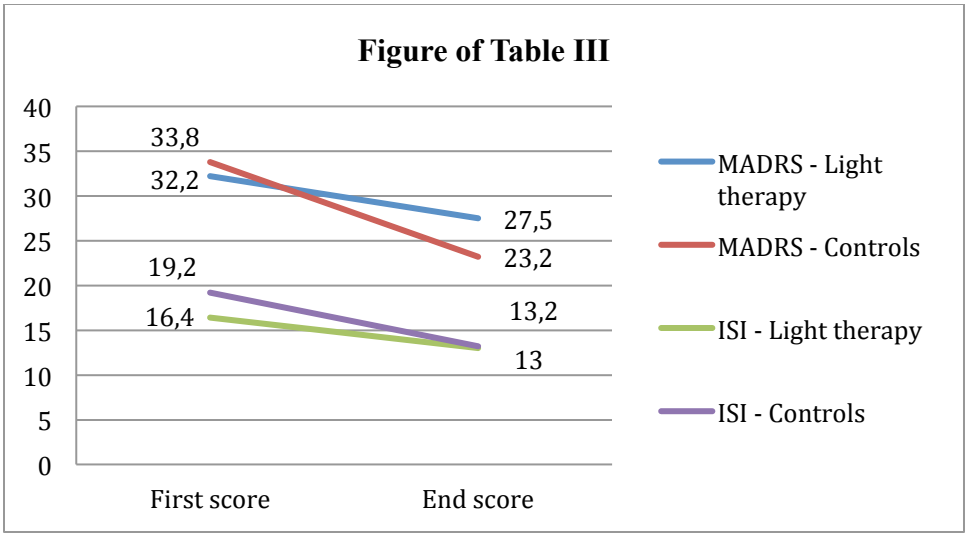
Variable	Light therapy n=18	Controls n=36
MADRS 1st score	32.2±13.0	33.8±9.7[b]
MADRS end score	27.5±13.7[a]	23.2±11.3[c]
ISI 1st score	16.4±6.3	19.2±6.6[c]
ISI 1 end score	13.0±7.6[a]	13.2±7.3[c]

a) n=17, b) n=31, c) n=28

Insomnia Severity Index

The ISI end score for the light therapy group and the control group are displayed in tables II and III. In total, 17 out of 18 patients in the light therapy group and 28 out of 36 in the control group self-rated themselves before leaving the department. The mean ISI end score was 13.00 points for the light therapy group and 13.18 for the control group. This makes a difference of 0.18 points, or 1 % lower score for the patients who had received the light therapy treatment.

Table III shows the first and last ISI scores of the hospital stay. The mean 1st ISI score was 16.44 for the light therapy group and 19.21 for the control group, which means that the light therapy group improved 3.44 points or 21 % during their stay, whereas the control group improved 6.03 points or 31 %. These results are not statistically significant.



This figure of Table III compares the Light therapy group's and the Control group's results and improvements of the self-scoring questionnaires MADRS-s (for depression) and ISI (for insomnia) during the hospital stay.

Psychiatric medication

The percentage of patients taking psychiatric medication in the light therapy group and the control group are displayed in table IV. All of the 18 patients in the light therapy group and 35 out of 36 in the control group were medicated with a therapeutic dose of one or more antidepressants. None of the patients in the light therapy group were taking antipsychotics and 2 out of 36 in the control group were medicated with an antipsychotic (but not as primary treatment). Out of the 18 patients in the light therapy group 6 (33 %) were under treatment with mood stabilizers (5 of these with quetiapin) and in the control group 4 out of the 36 (11 %) were under treatment with mood stabilizers (2 with quetiapin). 89 % in the light therapy group were taking hypnotics, and 92 % in the control group. In both groups 89 % were taking some form of sedatives.

Table IV – Psychiatric medication during the hospital stay

Variable	Light therapy n=18	Controls n=36
Antidepressants	100 %	97 %
Antipsychotics	0 %	6 %
Mood stabilizers	33 %	11 %
Hypnotics	89 %	92 %
Sedatives	89 %	89 %

Table 5 shows that the control group consumed benzodiazepines converted to diazepam in greater quantities than the light therapy group. The accumulated dose for the whole hospital stay for the control group was 99.8 mg and 75.2 for the light therapy group, 75 % of the control group's consumption. The light therapy group consumed 4.3 mg/day and the control group 4.8 mg/day, 11 % more than the light therapy group.

Table V – Consumed benzodiazepines converted to diazepam during the hospital stay

Variable	Light therapy n=18	Controls n=36
Mg/hospital stay	39.1±15.9	38.8±16.5
Mg/day	72 %	72 %

Discussion

This study indicates a possible faster improvement as the light therapy group stayed three days shorter than the control group. The mean length of stay was 16 days for the light therapy group and 19 for the control group. These results point towards the same conclusion in a double blinded study where more rapid improvement were found, but also more profound improvements of major depression (30 %) which this study does not show [38]. Howeve[r it is not possible to interpret these findings due to the low statistical power, and it is even harder do draw any conclusions when the MADRS-S scores are lower at start in the light therapy group compared to the control group but higher at the end of treatment. The mean MADRS-S end score was 27 points for the light therapy group and 23 for the control group. This is somewhat contradictory.

One possible reason may be the fact that 94 % of the patients in the light therapy group answered the end questionnaire, but only 78 % of the control group, and those who did not want to rate themselves were dissatisfied with their stay and would have given a higher score. The attending physician has in any case assessed the patients as ready for discharge, which would indicate that they felt well enough and had improved in their depression.

It is interesting how the patients in the light therapy group 5 times as often were given quetiapin compared with the control group. This could be explained by new treatment routines. Quetiapin has become more popular to give in a mood stabilizing purpose, and the control group was identified from data reaching from 2010 to 2013, and light therapy started 1 October 2013. It is also interesting that light therapy may reduce the use of benzodiazepines. The total accumulated dose of diazepam equivalent of benzodiazepine for the whole hospital stay for the control group was 100 mg and 75 for the light therapy group. The daily average dosage was 4.8 respectively 4.3 mg/day. These results may be secondary to higher use of quetiapin and there is difficult to make any conclusions with the low statistical power.

However, discrepancy between all demographic variables except age and gender are vast, especially whether the patient is owner of his/her own home or not. Since all patients who have received treatment with light therapy have had the choice to choose whether they want light therapy or not and the control group were chosen based on whether they could theoretically be offered therapy or not, this study includes patient in the control group who are suited for light therapy but would have said no to receive light therapy in real life. There may be variables that have not been considered or are hard to detect in the patients records, which could be crucial for whether a patient is suitable or not for light therapy.

To make the light therapy group and the control group more homogeneous it would have been possible to only choose patients to the control group who had been admitted during the same time of the year as the patients who received light therapy and narrow down the ICD-codes and. For instance if only patients with moderate and severe depressive episode were allowed to be in the study. However, this would have reduced the numbers of patients in both the light therapy group and the control group even more, which would have led to even more difficulties to interpret the results and get any significant results.

This study is limited both due to a small number of patients in both groups and due to the retrospectively collected data from the patient records resulting in missing data and possible inaccuracy in interpretation of data due to human error. In the future a randomized control study where patients are randomly allocated to either receive chronobiological treatment or some other kind of treatment (for example sleep hygiene) would solve this problem. It would even be possible to make the study blinded by for instance giving the control group dim light instead of bright light [32], [33].

Other ways to improve the conditions of future chronobiological projects could be to look over the self-assessment questionnaires. One way would be to translate the Morningness-Eveningness Questionnaire (MEQ) from English to Swedish for more correct results estimations of melatonin levels [37]. Even though no patient in this study seemed to be bothered by this questionnaire being in English and that the nursing staff could help to

translate questions if needed, a Swedish version of MEQ would be helpful future patients. Also an additional questionnaire to rate depression could be The Hamilton Rating Scale for Depression (HAM-D) for better possibilities to compare results with from other studies on light therapy [32], [33].

It would also be interesting not only to measure results from self-rating scales but also to measure the serum levels of the hormones melatonin and cortisol and possible changes of these before, during and after treatment, since these hormones diurnal rhythmic fluctuations and serum levels often change during a depressive episode [6], [7]. This would give an objective evaluation of how light therapy affect the circadian rhythm in patients with depression. However, this would increase the costs of the project vastly as several measurements of the serum levels each day would be necessary. This would also be an invasive and possibly a bothersome moment for the patients.

Conclusion

This study could not present a statistically significant more rapid improvement in depressive self-scoring and insomnia. Though, it provides support to continue studying light therapy in patients with affective disorder, just like Socialstyrelsen recommends [1]. A randomized control trial with a higher number of patients would have better qualifications to get results with high statistical power. It would also be interesting if such a study looked into the use of diazepam, and if it would be possible to decrease the use of this drug with light therapy.

Populärvetenskaplig sammanfattning på svenska

Det finns starka samband mellan sömn och depression. Sömnbesvär ses som ett av kärnsymptomen hos deprimerade patienter. För lite ljus kan ge negativa effekter på hjärnan och depression kan spegla en rubbning av hormoner och signalsubstanser som styr sömn-vakenhetscykeln.

Det finns forskning som visar att ljusterapi tillsammans med läkemedelsbehandling har positiv effekt på depression. Teorin är att genom ljusterapi som simulerar dagsljuset kan kroppens produktion av hormonet melatonin styras för att få dygnsrytmen i fas, förbättra sömn och lindra depressiva besvär. Socialstyrelsen önskar ytterligare forskning på området med ljusbehandling innan de vill rekommendera svenska sjukhus att använda ljusbehandling för deprimerade patienter.

Ljusbehandling går till så att patienten på morgonen sitter bekvämt framför ljuslampan på 15-20 cm avstånd under 30 minuter. Ljuslampan filtrerar bort UV-ljus och lyser med en effekt på 10,000 lux. Detta kan jämföras med solens belysning med 100,000 lux en solig sommardag och 250-500 lux inomhus med normal takbelysning.

I studien jämfördes patienter som fått ljusbehandling och patienter som inte har fått det gällande psykisk hälsa, sömn, medicinering samt vårdtid. Detta har varit möjligt eftersom det finns resultat från skattningsformulär för sömnbesvär och depressiva besvär för alla patienter sedan flera år tillbaka på avdelningen i patientjournaler.

Vi tittade på de första 20 patienterna som genomgått ljusbehandling men två avbröt behandlingen och jämförde de 18 kvarstående med 36 patienter som uppfyllde alla krav för ljusbehandling, men som vårdades innan behandlingsmetoden infördes som rutin på avdelningen.

Studien kunde dock inte med statistisk säkerhet visa att ljusbehandling skulle leda till kortare vårdtid, snabbare och större förbättring av depressiva besvär och sömnbesvär eller

minska intaget av lugnande medicin. Det vill säga, man kan inte utesluta att slumpen är mer avgörande än ljusbehandlingen för resultaten. Vissa av resultaten pekar dock på att ljusbehandling möjligtvis kan leda till snabbare förbättring och mindre användning av vissa lugnande läkemedel, men å andra sidan pekar andra resultat på att de som inte fått ljusbehandling förbättrades mer och mådde bättre vid utskrivning än de som hade fått ljusbehandling.

Det vore intressant att fortsatt i framtiden göra en kontrollerad studie med fler patienter där man lottar patienterna om de ska få ljusbehandling eller inte. Då kan man få säkrare resultat, mer styrka i studien och bättre svar på de frågor vi ställt.

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References

1. Socialstyrelsen Nationella riktlinjer för vård vid depression och ångestsyndrom 2010 Artikelnummer: 2010-3-4 ISBN: 978-91-86301-94-1
2. Tsuno N, Besset A, Ritchie K_ Sleep and depression. J Clin Psych 2005;66, 1254-1269
3. Aragun MY, Kara H, Solmaz M: Sleep disturbances and suicidal behaviour in patients with major depression. J Clin Psych 1997;58, 279-251
4. Franzen PL, Buysse D: Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. Dia Clin Neurosci 2008; 10, 473-481.
5. Mizukawa R, Ishiguro S, Takada H, Kishimoto A, Ogura C, Hazama H. Long-term observation of a manic-depressive patient with rapid cycles. Biol Psychiatry. 1991 Apr 1;29(7):671-8. No abstract available.
6. Bernard J. Carroll et al, Urinary free Cortisol excretion in depression, Psychological Medicine (1976), 6: 43-50
7. Germain A, Kupfer DJ. Circadian rhytm disturbances in depression. Hum Psychopharmacol Clin Exp 2008; 23, 571-585.
8. Wehr TA, Wirz-Justice A, Goodwin FK, Duncan W, Gillin JC. Phase advance of the circadian sleep-wake cycle as an antidepressant. Science. 1979 Nov 9;206(4419):710-3.
9. Hastings MH, Maywood ES, Reddy AB. Two decades of circadian time. J Neuroendocrinol. 2008 Jun;20(6):812-9. doi: 10.1111/j.1365-2826.2008.01715.x. Review.
10. Czeisler CA, Gooley JJ. Sleep and circadian rhythms in humans. Cold Spring Harb Symp Quant Biol. 2007;72:579-97. doi: 10.1101/sqb.2007.72.064. Review.
11. Challet E. Minireview: Entrainment of the suprachiasmatic clockwork in diurnal and nocturnal mammals.Endocrinology. 2007 Dec;148(12):5648-55. Epub 2007 Sep 27. Review.

12. Lewy AJ. Melatonin and human chronobilology. Cold Spring Harb Symp Quant Biol 2007;148, 623-636.
13. Cajochen C, Kräuchi K, Wirz-Justice A. Role of melatonin in the regulation of human circadian rhythms and sleep. J Neuroendocrinol. 2003 Apr;15(4):432-7. Review.
14. Minors DS, Waterhouse JM, Wirz-Justice A. A human phase-response curve to light. Neurosci Lett. 1991 Nov 25;133(1):36-40.
15. Khalsa SB, Jewett ME, Cajochen C, Czeisler CA. A phase response curve to single bright light pulses in human subjects. J Physiol. 2003 Jun 15;549(Pt 3):945-52. Epub 2003 Apr 25.
16. Burgess HJ, Revell VL, Eastman CI. J Physiol. 2008 Jan 15;586(2):639-47. A three pulse phase response curve to three milligrams of melatonin in humans. Epub 2007 Nov 15. Erratum in: J Physiol. 2008 Mar 15;586(6):1777.
17. Fuller PM, Gooley JJ, Saper CB. Neurobiology of the sleep-wake cycle: sleep architecture, circadian regulation, and regulatory feedback. J Biol Rhythms. 2006 Dec;21(6):482-93. Review.
18. Hastings MW, Maywood ES, Reddy AB. Two decades of circadian time. J Neuroendoccinol 2008;20, 812-819.
19. Wirtz-Justice A. Biological rhym disturbances in mood disorders. Int Clin Psychupharmacol 2006;21, S11-15.
20. Chronotherapeutics (light and wake therapy) in affective disorders.
Wirz-Justice A, Benedetti F, Berger M, Lam RW, Martiny K, Terman M, Wu JC. Psychol Med. 2005 Jul;35(7):939-44.
21. Stahl S.: Stahl`s essential psychopharmacology.The prescriber`s guide. Antidepressants. Cambridge Univ Press 2013.
22. 2. Aragun MY, Kara H, Solmaz M: Sleep disturbances and suicidal behaviour in patients with major depression. J Clin Psych 1997;58, 279-251

23. Quera Salva MA, Vanier B, Laredo J, Hartley S, Chapotot F, Moulin C, Lofaso F, Guillemault C: Major depressive disorder, sleep EEG and agomelatine: an open-label study. Int J Neuropscychophar 2007; 10, 691-696.
24. 8. NICE. Insomnia-newer hypnotic drugs. Zaleplon, zolpidem and zopliclone for the management of insomnia. 2004. http://www.nice.org.uk
25. Wirz-Justice A, Benedetti F, Terman M: Chronotherapeutics for Affective Disorders. Karger 2009.
26. Benedetti F, Barbini B, Colombo C, Smeraldi E. Chronotherapeutics in a psychiatric ward. Sleep Med Rev. 2007 Dec;11(6):509-22. Epub 2007 Aug 3. Review.
27. Rosenthal NE, Sack DA, Gillin JC, Lewy AJ, Goodwin FK, Davenport Y, Mueller PS, Newsome DA, Wehr TA. Seasonal affective disorder. A description of the syndrome and preliminary findings with light therapy. Arch Gen Psychiatry. 1984 Jan;41(1):72-80.
28. Rosenthal NA, Sack DA, Gillin J et al. Seasonal Affective Disorder. A description of the syndrome and preliminary findigs with light therapy. Arch Gen Psych 1984;41, 72-80.
29. Terman M, Terman JS. Light therapy for seasonal and nonseasonal depression: efficacy, protocol, safety, and side effects. CNS Spectr. 2005 Aug;10(8):647-63; quiz 672. Review.
30. Kripke DF, Mullaney DJ, Atkinson M, Wolf S. Circadian rhythm disorders in manic-depressives. Biol Psychiatry. 1978 Jun;13(3):335-51.
31. Tuunainen A, Kripke DF, Endo T. Light therapy for non-seasonal depression. Cochrane Database Syst Rev 2004;2, CD004050.
32. Benedetti F, Colombo C, Pontiggia A, Bernasconi A, Florita M, Smeraldi E. Morning light treatment hastens the antidepressant effect of citalopram: a placebo-controlled trial. J Clin Psychiatry. 2003 Jun;64(6):648-53.
33. Martiny K. Adjunctive bright light in non-seasonal major depression. Acta Psychiatr Scand Suppl. 2004;(425):7-28.

34. Szabo Z, Antal A, Tokaji Zs, Kalman J et al. Light therapy increases visual contrast sensitivity in seasonal affective disorder. Psych Res 2004;126, 15-21.
35. Szabo Z, Tokaji Zs, Kalman J, Oroszi L et al. The effect of light exposure on pupillary fluctuations in healthy subjects. J Affec Dis 2004;78, 153-156.
36. Wirz-Justice, Benedetti, Terman, Chronotherapeutics for Affective Disorder A Clinician's Manual for Light and Wake Therapy 2nd, revisededition, 2013
37. Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. Int J Chronobiol. 1976;4(2):97-110.
38. Benedetti F, Colombo C, Pontiggia A, Bernasconi A, Florita M, Smeraldi E. Morning light treatment hastens the antidepressant effect of citalopram: a placebo-controlled trial. J Clin Psychiatry. 2003 Jun;64(6):648-53.

MADRS SJÄLVSKATTNING

Namn	Personnummer	Datum

Det är helt frivilligt att besvara frågorna i formuläret. Genom att besvara dem ger du ditt samtycke till att din behandlare får ta del av resultatet. Avsikten med frågorna är att få en detaljerad bild av hur du mår psykiskt. Du och din behandlare kommer att diskutera resultaten, som kan ha betydelse för val av behandling.

Frågorna innehåller en rad olika påståenden om hur man kan må i olika avseenden. Påståendena uttrycker på en skala 0-6 olika grader av psykiska besvär, alltifrån frånvaro av besvär (0 poäng) till maximalt uttalade besvär (6 poäng). Sätt en ring runt siffran som du tycker bäst stämmer överens med hur du mått de senaste tre dagarna. Tänk inte allt för länge, utan försök att svara spontant.

KOM IHÅG, att bedömningen endast gäller de senaste tre dagarna.

1. Sinnesstämning

Här ber vi dig beskriva din sinnesstämning, om du känner dig ledsen, tungsint eller dyster till mods. Tänk efter hur du har känt dig de senaste tre dagarna, om du har skiftat i humöret eller om det har varit i stort sett detsamma hela tiden, och försök särskilt komma ihåg om du har känt dig lättare till sinnes om det har hänt något positivt.

0 Jag kan känna mig glad eller ledsen, allt efter omständigheterna.
1
2 Jag känner mig nedstämd för det mesta, men ibland kan det kännas lättare.
3
4 Jag känner mig genomgående nedstämd och dyster. Jag kan inte glädja mig åt sådant som vanligen skulle göra mig glad.
5
6 Jag är totalt nedstämd och olycklig att jag inte kan tänka mig värre.

2. Oroskänslor

Här ber vi dig markera i vilken utsträckning du har haft känslor av inre spänning, olust och ångest eller odefinierad rädsla under de senaste tre dagarna. Tänk särskilt på hur intensiva känslorna varit, och om de kommit och gått eller funnits hela tiden.

0 Jag känner mig mestadels lugn.
1
2 Ibland har jag obehagliga känslor av inre oro.
3
4 Jag har ofta en känsla av inre oro som ibland kan bli mycket stor, och som jag måste anstränga mig för att bemästra.
5
6 Jag har fruktansvärda, långvariga eller outhärdliga ångestkänslor.

3. Sömn

Här ber vi dig beskriva hur bra du sover. Tänk efter hur länge du sovit och hur god sömnen varit under de senaste tre nätterna. Bedömningen skall avse hur du faktiskt sovit, oavsett om du tagit sömnmedel eller ej. Om du sover mer än vanligt, sätt din markering vid 0.

0 Jag sover lugnt och bra och tillräckligt länge för mina behov. Jag har inga särskilda svårigheter att somna.
1
2 Jag har vissa sömnsvårigheter. Ibland har jag svårt att somna eller sover ytligare eller oroligare än vanligt.
3
4 Jag sover minst två timmar mindre per natt än normalt. Jag vaknar ofta under natten, även om jag inte blir störd.
5
6 Jag sover mycket dåligt, inte mer än 2-3 timmar per natt.

4. Matlust

Här ber vi dig ta ställning till hur din aptit är, och tänka efter om den på något sätt skilt sig från vad som är normalt för dig. Om du skulle ha bättre aptit än normalt, markera då det på 0.

0 Min aptit är som den brukar vara.
1
2 Min aptit är sämre än vanligt.
3
4 Min aptit har nästan helt försvunnit.
5
6 Jag vill inte ha någon mat. Om jag skall få någonting i mig, måste jag övertalas att äta.

Summa denna sida:

KOM IHÅG, att bedömningen endast gäller de senaste tre dagarna.

5. Koncentrationsförmåga

Här ber vi dig ta ställning till din förmåga att hålla tankarna samlade och koncentrera dig på olika aktiviteter. Tänk igenom hur du fungerar vid olika sysslor som kräver olika grad av koncentrationsförmåga, t ex läsning av komplicerad text, lätt tidningstext och TV-tittande.

0 Jag har inga koncentrationssvårigheter.
1
2 Jag har tillfälligt svårt att hålla tankarna samlade på sådant som normalt skulle fånga min uppmärksamhet (t ex läsning eller TV-tittande).
3
4 Jag har påtagligt svårt att koncentrera mig på sådant som normalt inte kräver någon ansträngning från min sida (t ex läsning eller samtal med andra människor).
5
6 Jag kan överhuvudtaget inte koncentrera mig på någonting.

6. Initiativförmåga

Här ber vi dig försöka värdera din handlingskraft. Frågan gäller om du har lätt eller svårt för att komma igång med sådant du tycker du bör göra, och i vilken utsträckning du måste övervinna ett inre motstånd när du skall ta itu med något.

0 Jag har inga svårigheter med att ta itu med nya uppgifter.
1
2 När jag skall ta itu med något, tar det emot på ett sätt som inte är normalt för mig.
3
4 Det krävs en stor ansträngning för mig att ens komma igång med enkla uppgifter som jag vanligtvis utför mer eller mindre rutinmässigt.
5
6 Jag kan inte förmå mig att ta itu med de enklaste vardagssysslor.

7. Känslomässigt engagemang

Här ber vi dig ta ställning till hur du upplever ditt intresse för omvärlden och för andra människor, och för sådana aktiviteter som brukar bereda dig nöje och glädje.

0 Jag är intresserad av omvärlden och engagerar mig i den, och det bereder mig både nöje och glädje.
1
2 Jag känner mindre starkt för sådant som brukar engagera mig. Jag har svårare än vanligt att bli glad eller svårare att bli arg när det är befogat.
3
4 Jag kan inte känna något intresse för omvärlden, inte ens för vänner och bekanta.
5
6 Jag har slutat uppleva några känslor. Jag känner mig smärtsamt likgiltig även för mina närmaste.

6. Pessimism

Frågan gäller hur du ser på din egen framtid och hur du uppfattar ditt eget värde. Tänk efter i vilken utsträckning du ger dig självförebråelser, om du plågas av skuldkänslor, och om du oroat dig oftare än vanligt för t ex din ekonomi eller din hälsa.

0 Jag ser på framtiden med tillförsikt. Jag är på det hela taget ganska nöjd med mig själv.
1
2 Ibland klandrar jag mig själv och tycker att jag är mindre värd än andra.
3
4 Jag grubblar ofta över mina misslyckanden och känner mig mindervärdig eller dålig, även om andra tycker annorlunda.
5
6 Jag ser allting i svart och kan inte se någon ljusning. Det känns som om jag var en alltigenom dålig människa, och som om jag aldrig skulle kunna få någon förlåtelse för det hemska jag gjort.

9. Livslust

Frågan gäller din livslust, och om du känt livsleda. Har du tankar på självmord, och i så fall, i vilken utsträckning upplever du detta som en verklig utväg?

0 Jag har normal aptit på livet.
1
2 Livet känns inte särskilt meningsfullt men jag önskar ändå inte att jag vore död.
3
4 Jag tycker ofta det vore bättre att vara död, och trots att jag egentligen inte önskar det, kan självmord ibland kännas som en möjlig utväg.
5
6 Jag är egentligen övertygad om att min enda utväg är att dö, och jag tänker mycket på hur jag bäst skall gå tillväga för att ta mitt eget liv.

NEDANSTÅENDE FYLLS I AV VÅRDPERSONAL

Summa denna sida:	
Summa föregående sida:	
Totalpoäng:	

Insomnia Severity Index (ISI)

Bedöm hur pass allvarliga dina sömnsvårigheter har varit de senaste två veckorna.

Svårigheter	*Inga*	*Små*	*Medel*	*Stora*	*Mycket stora*
1. Somna på kvällen	0	1	2	3	4
2. Vakna upp under natten	0	1	2	3	4
3. Vakna för tidigt på morgonen	0	1	2	3	4

4. Hur missnöjd är du med ditt nuvarande sömnmönster?

Mycket nöjd	*Nöjd*	*Varken eller*	*Missnöjd*	*Mycket missnöjd*
0	1	2	3	4

5. I hur pass hög grad anser du att dina sömnsvårigheter stör dig i din vardag (t.ex. trötthet, arbete, fritid, koncentration, minne och humör)?

Inte alls störande	*Lite störande*	*Något störande*	*Klart störande*	*Mycket störande*
0	1	2	3	4

6. I hur pass hög grad tror du att andra personer märker av att dina sömnsvårigheter försämrar din livskvalitet?

Inte alls märkbart	*Lite märkbart*	*Något märkbart*	*Klart märkbart*	*Mycket märkbart*
0	1	2	3	4

7. Hur oroad är du över dina nuvarande sömnsvårigheter?

Inte alls oroad	*Lite oroad*	*Något oroad*	*Klart oroad*	*Mycket oroad*
0	1	2	3	4

ISI = Insomnia Severity Index (Morin. 1993).

MORNINGNESS-EVENINGNESS QUESTIONNAIRE (MEQ)

Instructions:

- Please read each question very carefully before answering.
- Please answer each question as honestly as possible.
- Answer ALL questions.
- Each question should be answered independently of others. Do NOT go back and check your answers.

1. What time would you get up if you were entirely free to plan your day?

5:00 – 6:30 AM	5
6:30 – 7:45 AM	4
7:45 – 9:45 AM	3
9:45 – 11:00 AM	2
11:00 AM – 12 NOON	1
12 NOON – 5:00 AM	0

2. What time would you go to bed if you were entirely free to plan your evening?

8:00 – 9:00 PM	5
9:00 – 10:15 PM	4
10:15 PM – 12:30 AM	3
12:30 – 1:45 AM	2
1:45 – 3:00 AM	1
3:00 AM – 8:00 PM	0

3. If there is a specific time at which you have to get up in the morning, to what extent do you depend on being woken up by an alarm clock?

Not at all dependent	4
Slightly dependent	3
Fairly dependent	2
Very dependent	1

4. How easy do you find it to get up in the morning (when you are not woken up unexpectedly)?

Not at all easy	1
Not very easy	2
Fairly easy	3
Very easy	4

5. How alert do you feel during the first half hour after you wake up in the morning?

Not at all alert	1
Slightly alert	2
Fairly alert	3
Very alert	4

6. How hungry do you feel during the first half-hour after you wake up in the morning?

Not at all hungry	1
Slightly hungry	2
Fairly hungry	3
Very hungry	4

7. During the first half-hour after you wake up in the morning, how tired do you feel?

Very tired	1
Fairly tired	2
Fairly refreshed	3
Very refreshed	4

8. If you have no commitments the next day, what time would you go to bed compared to your usual bedtime?

Seldom or never later	4
Less than one hour later	3
1-2 hours later	2
More than two hours later	1

9. You have decided to engage in some physical exercise. A friend suggests that you do this for one hour twice a week and the best time for him is between 7:00 – 8:00 am. Bearing in mind nothing but your own internal "clock", how do you think you would perform?

Would be in good form	4
Would be in reasonable form	3
Would find it difficult	2
Would find it very difficult	1

10. At what time of day do you feel you become tired as a result of need for sleep?

8:00 – 9:00 PM	5
9:00 – 10:15 PM	4
10:15 PM – 12:45 AM	3
12:45 – 2:00 AM	2
2:00 – 3:00 AM	1

11. You want to be at your peak performance for a test that you know is going to be mentally exhausting and will last for two hours. You are entirely free to plan your day. Considering only your own internal "clock", which ONE of the four testing times would you choose?

8:00 AM – 10:00 AM	4
11:00 AM – 1:00 PM	3
3:00 PM – 5:00 PM	2
7:00 PM – 9:00 PM	1

12. If you got into bed at 11:00 PM, how tired would you be?

Not at all tired	1
A little tired	2
Fairly tired	3
Very tired	4

13. For some reason you have gone to bed several hours later than usual, but there is no need to get up at any particular time the next morning. Which ONE of the following are you most likely to do?

Will wake up at usual time, but will NOT fall back asleep	4
Will wake up at usual time and will doze thereafter	3
Will wake up at usual time but will fall asleep again	2
Will NOT wake up until later than usual	1

14. One night you have to remain awake between 4:00 – 6:00 AM in order to carry out a night watch. You have no commitments the next day. Which ONE of the alternatives will suite you best?

Would NOT go to bed until watch was over	1
Would take a nap before and sleep after	2
Would take a good sleep before and nap after	3
Would sleep only before watch	4

15. You have to do two hours of hard physical work. You are entirely free to plan your day and considering only your own internal "clock" which ONE of the following time would you choose?

8:00 AM – 10:00 AM	4
11:00 AM – 1:00 PM	3
3:00 PM – 5:00 PM	2
7:00 PM – 9:00 PM	1

16. You have decided to engage in hard physical exercise. A friend suggests that you do this for one hour twice a week and the best time for him is between 10:00 – 11:00 PM. Bearing in mind nothing else but your own internal "clock" how well do you think you would perform?

Would be in good form	1
Would be in reasonable form	2
Would find it difficult	3
Would find it very difficult	4

17. Suppose that you can choose your own work hours. Assume that you worked a FIVE hour day (including breaks) and that your job was interesting and paid by results). Which FIVE CONSECUTIVE HOURS would you select?

5 hours starting between 4:00 AM and 8:00 AM	5
5 hours starting between 8:00 AM and 9:00 AM	4
5 hours starting between 9:00 AM and 2:00 PM	3
5 hours starting between 2:00 PM and 5:00 PM	2
5 hours starting between 5:00 PM and 4:00 AM	1

18. At what time of the day do you think that you reach your "feeling best" peak?

5:00 – 8:00 AM	5
8:00 – 10:00 AM	4
10:00 AM – 5:00 PM	3
5:00 – 10:00 PM	2
10:00 PM – 5:00 AM	1

19. One hears about "morning" and "evening" types of people. Which ONE of these types do you consider yourself to be?

Definitely a "morning" type	6
Rather more a "morning" than an "evening" type	4
Rather more an "evening" than a "morning" type	2
Definitely an "evening" type	0

VÄSTRA GÖTALANDSREGIONEN

Bilaga 2

Ekvivalenta doser

5 mg diazepam – Stesolid
15 mg oxazepam – Sobril
2,5 mg nitrazepam - Nitrazepam
1 mg lorazepam - Temesta
0,5 mg triazolam - Halcion
0,5 mg alprazolam - Xanor
0,5 mg flunitrazepam – Flunitrazepam

Tabell 2. Vanliga missbrukade bensodiazepiner – tid till tillslag, halveringstid och ekvivalenta doser

Läkemedel	Tmax b) (timmar)	Eliminationstid c)	Dos ekvivalent med 5 mg diazepam (mg) a)
Klonazepam	1–4	Lång	0,25
Triazolam	1,7	Kort	0,25
Alprazolam	1	Kort	0,5
Flunitrazepam	1	Kort	0,5
Lorazepam	1–2	Kort	1,0
Nitrazepam	1,5	Kort	2,5
Diazepam	1	Lång	5,0
Oxazepam	2	Kort	15,0

a) Missbrukspotentialen är främst relaterad till två variabler: affiniteten för receptorn, respektive snabbheten i tillslaget. Högre affinitet motsvaras (för en full agonist) av en lägre ekvipotent dos, här angiven i dosekvivalenter diazepam.
b) Tid till tillslag anges här som antal timmar till maximal plasmakoncentration
c) Ackumulationsrisken är relaterad till eliminationshalveringstiden, här grovt klassificerad som lång (> 24 timmar) respektive kort (< 24 timmar).

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