On The Bright Side of Life - The Effect of Ambient Light Intensity on Postsurgical Patient-Reported Outcomes

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1On the bright side of life -

2The effect of ambient light intensity on postsurgical patient-reported outcomes

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21

1Abstract:

2Light intensity affects humans in multiple ways. We aimed to characterize the potential
3impact of light intensity on patients' pain management experience in the perioperative setting.
4Within the German multicenter registry project QUIPS, we collected patient reported
5outcomes (PROs) concerning pain and side effects, demographics and perioperative pain
6medication, and measured the light intensity in their rooms on the first postoperative day.
7Primary endpoint was maximum pain intensity rated on the numerical rating scale (NRS, 0-
810). Secondary endpoints were pain intensity during movement, mood, nausea, tiredness
9and satisfaction. Measurement of light intensity was done with a calibrated light meter. For
10analysis, we used linear and log-linear regression models with age, gender, pre-existing
11chronic pain, ASA status, and logarithmized light intensity as independent variables. Data of
12539 surgical patients from 9 hospitals were included. We found no significant effect of light
13intensity on the primary endpoint. However, we observed a strong positive correlation
14between nausea and light intensity.

15Perspective: Our study indicates that further investigations about the clinical importance of
16light exposure with regard to nausea and other medical conditions are worthwhile.

17

18Key words:

19postoperative pain, light exposure, nausea, patient-reported outcomes (PROMs)

20

21Trial registration:

22QUIPS is registered in the German Clinical Trials Register (DRKS00006153)

23

24Ethics approval:

25QUIPS was approved by the Jena University Hospital's ethics committee (Ref.: 2722 –

2612/09). We confirm that all included participants signed an informed consent and the study

27was performed in accordance to the guidelines of the declaration of Helsinki.

1Introduction

2Light is defined as optical radiation entering the eye that provides visual sensation in
3humans. The effects of light fall into two categories: those modifying the individual endocrine,
4hormone, and metabolic state by light reaching the retina and those resulting from light on
5the skin. According to this specific vision related definition, light has been increasingly related
6to a range of ocular circadian, neuroendocrine, neurobehavioral and therapeutic responses
7in humans. These responses are driven primarily by stimulation of photosensitive retinal
8ganglion cells (pRGCs) that are most sensitive to short-wavelength (app. 480 nm) blue
9light[2]. Exposure to natural sunlight has been associated with improvement in mood,
10reduced mortality and decreased stress, pain and analgesic medication use and pain
11medication cost in patients who have undergone spinal surgery.[3] Among hormonal effects
12by light, the (reduced) secretion of melatonin from the pineal gland is the most important.
13Moreover, the activity of serotonin n-acetyltransferase is reduced after exposure to light.
14While light exposure elevates the serotonin levels and likewise reduces melatonin levels,
15serotonin might most likely act as a modulator of pain in the central nervous system.[4]
16Serotonin is a significant modulator of sensory input to the central nervous system; however,
17the only analgesics that selectively target G-protein-coupled 5-HT receptors are highly
18specific for treatment of headache.[4] Previous work has indicated that serotonin can both
19potentiate and inhibit primary afferent neurotransmission, and given that most subtypes of
205HT receptor are present in sensory ganglia, serotonin potentially has both pro- and
21antinociceptive effects through modulation of primary afferent neurotransmission.
22Postoperative pain is a major problem of modern medicine, confronting every hospital with
23structural, procedural and financial challenges. Extensive studies have demonstrated that
24many patients suffer from moderate to severe postoperative pain.[5],[6] Severe pain is
25associated with decreased patient satisfaction, delayed postoperative ambulation, increased
26incidence of chronic postoperative pain,[7] pulmonary [8], [9] and cardiac complications[10]
27and increased morbidity and mortality[11]. Options for treatment of acute, postoperative, as

1well as for chronic pain, are limited, and many drugs are marginally effective [13] and often
2accompanied by severe side effects.

3Non-pharmacological options for the treatment of pain would be highly desirable and
4advantageous in safety, including lack of tolerance, somnolence, addiction, gastrointestinal
5disturbances and, perhaps, other factors such as convenience and cost. Light therapy has
6been reported to be useful for multiple medical conditions [14], for example to control
7depression,[15], [16] to increase daytime circadian stimulation, to improve sleep quality, and
8mitigate depression in Alzheimer disease[17]. Exposing patients to bright light of more than
96000 lux significantly improved seasonal affective disorder, a serious condition with
10increased risk of suicidality. An association has also been found between staying in a sunny
11room and a decreased need for analgesic medication following surgery. Patients who were
12accommodated on the bright side of the hospital perceived less stress and required less
13analgesic medication than those on the dark side [18]. In addition, a market for substance
14free alternatives to relieve pain emerged, including light based products like LED-belts for
15back pain treatment.

16These findings indicate a physiological relationship of pain perception and lighting condition.
17However, this relationship has not yet been studied in a larger number of patients. Therefore,
18the main objective of this study was to observe a potential association between ambient light
19intensity and pain-related patient-reported outcomes (PROs) in clinical postoperative
20routines.

21

22

23**Methods**

24**Study design**

25This study was based on a prospective German multicentre registry named QUIPS (Quality
26Improvement in Postoperative Pain Treatment), which was started as a benchmark initiative
27to compare pain outcome parameters among participating German hospitals. The QUIPS
28project is supported by the German Societies and Professional Associations of

1anesthesiologists and surgeons [19]. Patients complete a validated 15-item QUIPS
2questionnaire on the first postoperative day. Patient reported data were gathered along with
3information on the type of surgery, anesthesia and pain treatment. Data assessment was
4carried out by trained study personnel. Data were collected in a standardized manner in
5randomly selected patients, unknown to the medical staff before data collection.

6Patients were informed in written form as well as orally by the study personnel that data
7collection was voluntary and anonymous and that they could refuse to be included at any
8time. Informed consent was documented by filling in the questionnaire. The project was
9approved by the Ethics Committee as well as the Data Security Board of Jena University
10Hospital, Germany, and all participating sites obtained approval from their respective Ethics
11Committees.

12Outcome and Influencing Variables

13The primary outcome parameter was maximum pain intensity since surgery, measured with
14the numeric rating scale (NRS, 0=no pain, 10 = worst pain imaginable). Age, gender,
15preoperative chronic pain, pain during movement and ASA-score were selected as co-
16variables in the analysis [20]. The secondary endpoints were mood, nausea, tiredness and
17satisfaction. These items are also part of the validated 15-item QUIPS questionnaire. The
18outcome satisfaction has been rated on a scale from 0 to 10 (0= low grade,10 = highest
19grade) while the other secondary outcome parameters nausea, tiredness etc. have been
20determined binary (yes/no).

21

22Patients

23Nine hospitals participated in the study, and patients having completed the QUIPS
24questionnaire between August 2015 and September 2016 were included. Patients were
25included if the assessment was done on the day after surgery and if the patient was 18 years
26or older and able to understand the study. Exclusion criteria were the patient (1) had been
27transferred to another ward after surgery; (2) was not present in his room or had been

1discharged at the time of data collection; (3) refused to participate in the study; (4) could not
2communicate in German; (5) had cognitive deficits or (6) was sedated or asleep.

3

4**Light Measurement**

5The light measurement was done with calibrated light meters (unit: lx) by a hand-held device
6(model PCE-172, manufactured by PCE Instruments, Southampton, UK) in every
7participating site. The light meter captures the luminous flux per surface unit of measure
8independent from its direction and extensiveness. The sensor has a spectral sensitivity which
9is adapted to the human photopic luminosity curve. Light intensity measurement was only
10executed on days with constant weather conditions between 9 am and 5 pm. Days with
11frequent changes between sunshine and clouds were not included in the light study. The
12measurement was conducted all year round to include seasonal dependencies on light
13intensity. The measurement of light intensity was performed by placing the sensor at the foot
14of the patients' bed.

15

16**Statistical Analysis**

17**The analysis was performed using both logistic and linear regression models.** We used
18logarithmic transformation in order to describe the distribution of light intensity values.

19**The primary and secondary outcomes were considered as dependent variables. Age,**
20**sex and preoperative pain were used as independent factors. For Integration of**
21**variables into the regression model, inclusion method was applied. Furthermore we**
22used the same set of covariates including age, gender, chronic pain and asa score for our
23regression models.

24**A p value of 0.05 or lower was considered as significant. Data analyses were carried**
25**out using IBM SPSS Statistics version 24.0.**

26

1Results

2Data were collected from 539 surgical patients in 9 German hospitals for 14 months from
308/15 to 09/16. Demographic (sex, age, gender) and clinical data are shown in table 1. The
4mean worst pain intensity for all included patients since surgery was NRS of 5.7 while the
5mean light intensity measured averaged a worth of 946,76 lx (Table 2).

6

7Patient characteristics

age	median: 58 yrs	Q25 to 75: 55 to 75 yrs
gender	54.7 % female	44.3 % male
ASA 1	16.3 %	N=88
ASA2	50.3 %	N=271
ASA3	27.5 %	N=148

8**Table 1.** Age, gender and American Society of Anesthesiology (ASA) state of included patients

9

10Max. pain intensity and light intensity

	N	Minimum	maximum	mean	standard deviation
maximum pain (NRS 0-10)	537	0	10	5.74	2.73
log_light Value (lx)	539	24	25600	946.76	1875.59

11**Table 2.** Mean values of measured maximum pain intensity and light intensity in lx.

12

1Primary Outcome maximum pain

2

3For the primary endpoint maximum pain intensity, no significant effect of light intensity was
4found (table 3). Age ($p = 0,00$) and gender ($p = 0,01$) had a significant effect on the outcome
5maximum pain intensity after surgery.

6Primary outcome results

	coefficients not standardized univariate regression		standardized coefficients multivariable regression	significance
	Regression coefficient	standard error	Beta	
age	-0.05	0.01	-0.31	0.00
gender (male)	-0.69	0.24	-0.13	0.01
chronic pain	0.30	0.26	0.06	0.24
asa status	0.09	0.27	0.02	0.66
Log_light intensity	-0.09	0.25	-0.17	0.71

7**Table 3.** Summary of statistical relation between maximum pain and age, gender, pre-existing chronic
8pain and light intensity.

9

10Secondary Outcome – Tiredness, Satisfaction, Pain during movement

11

12For the secondary endpoints of pain intensity during movement, satisfaction and tiredness no
13significant effect of light intensity was found. Furthermore, the data showed a significant
14connection of gender and tiredness ($p = 0,00$, CI: 1,96 – 4,19), while pain during movement
15and age ($p = 0,00$, CI: 0,96 - 0,990) were statistically correlated.

16

17

18

1Secondary Outcome – Nausea

2A strong positive correlation between nausea and light intensity (Exp (B) = 2,63; $p < 0.05$, CI: 31,62 - 4,26) could be observed (table 4). The probability of a patient suffering from nausea 4rises by a factor of 2,6 per logarithmic light intensity value.

5Secondary outcomes results

	Regression coefficient	Standard error	Sig.	Exp (B)
age	-0.03	0.01	0.71	0.10
gender (male)	1.294	0.260	0.00	3.649
chronic pain	-0.371	0.251	0.140	0.690
ASA status	0.165	0.207	0.424	1.180
nausea	0.97	0.25	0.00	2.63

6**Table 4.** Statistical relation between secondary outcome variables nausea, age, gender, pre-existing 7chronic pain and light intensity.

8

9Discussion

10To our knowledge, this is the first analysis of an association between ambient light intensity 11and patient-reported outcome parameters related to postoperative pain management in a 12large number of patients in clinical routine. A former study evaluated the effect of sunlight on 13postoperative analgesic medication use and found that patients staying on the bright side of 14the hospital required 22 % less opioid equivalent compared to those on a dark side, 15suggesting a hypothetical connection of pain perception and light intensity. [3] Thus, it could 16be suggested that pain perception after surgery and light intensity might be connected. 17However, analgesic consumption is only a surrogate of pain after surgery that can be 18affected by many different factors. Since our data show no significant relation of light intensity 19with maximum pain perception as well as the secondary outcomes pain during movement,

1satisfaction and tiredness, the assumption of light intensity in patient rooms having an
2influence on patients' pain perception cannot be confirmed by our observational data.
3However, regarding the differences in sample size, study conditions and methods of the two
4studies no definite comparison can be made. While the former study included only patients
5undergoing spinal surgery, calculated mean light exposure by taking measurements twice a
6day five times each from three different points of the patients' room as well as having variant
7primary outcomes as pain medication use and cost, it is difficult to compare these two
8studies. [3]

9However, we found an unexpected positive correlation of daylight intensity and postoperative
10nausea. Up to date, there has not been any similar finding in other research concerning the
11connection of light and nausea. This finding might be explained with the metabolism of
12melatonin [21]. The sleep hormone secreted by the pituitary gland has various functions. As
13light exposure lowers the level of melatonin via downregulation of n-acetyltransferase, higher
14concentrations of its chemical precursor serotonin could result in clinical symptoms such as
15nausea, migraine and headache, mediated via 5-HT₃ and 5-HT_{1D} receptors. Migraine
16patients are known to suffer from hypersensitivity to light following lowered excitation
17thresholds in the central nervous system [22]. In addition, a more marked melatonin
18suppression after light exposure in migraine patients compared to controls suggests that the
19melatonin level plays a central role in the pathophysiology of migraine [23]. These findings
20emphasize the assumption that photoregulation of migraine headache is exerted by the non-
21image-forming retinal pathway that modulates the activity of dura-sensitive thalamocortical
22neurons [24]. Finally, a recent study has shown that melatonin functioning as a biomarker for
23circadian dysregulation correlated with major depression and fibromyalgia symptom severity
24[25]. These findings manifest the hypothesis that lighting has a severe effect on
25neurohumoral pain transmission and encourage further research.

26In context to our research design that emphasizes on acute postoperative pain there is no
27further evidence suggesting a significant effect of lighting conditions on pain intensity. Our
28findings could not provide further evidence on the main hypothesis. Explanation to our

1negative results could be the missing biological connection of the light effect organ skin and
2retina and the origin of acute pain that mainly results from structural damage and
3inflammation in the peripheral nervous system. Another reason presents itself in the delay of
4a potential effect due to the neurohumoral axis of melatonin regulation taking longer than a
5day to have a clinical measurable impact on pain.

6The significant correlation of higher light exposure and nausea in the postoperative setting
7should be subject of further research. Thus simple implementations regarding changes of the
8postoperative lighting conditions such as dimming of the ambient light appears to provide a
9preventive option for patients that are at risk of nausea.

10

11Specific limitations of the study include the following: 1) The measurement of light intensity
12occurred only once at the foot of the patients' beds. This process could methodologically be
13optimized considering affected light exposure intensity due to adjusted blinds, overhead
14lighting, artificial lighting or other confounding variables. For future research, it would be
15preferable to continuously measure light intensity variation in patient rooms during the whole
16day. 2) Due to the large patients sample size, a wide variety of different surgical patients that
17were exposed to various environmental conditions were included. 3) In the present study,
18only the room brightness (measured in lux) was determined. No difference was made
19between daylight and artificial light. Also the different color spectra of the different light
20sources and illuminants were not analyzed. Since individual colours can also cause different
21reactions, it would certainly make sense to include the distinction between daylight, artificial
22light and colour spectra of the individual artificial light sources in a further study.

23 4) As light is a complex phenomenon, having a biological impact that depends on spectrum,
24spatial distribution, timing and duration of exposure to the retina, there is a lack of valid
25methods of measurement up to date. While the current methods including light meters have
26a spectral sensitivity adjusted to the human photopic luminosity curve, modern
27measurements should consider that the photobiologic action spectre of the greatest
28importance to humans in order to stimulate non-image forming light detection system, ranges

1from 290 to 270 nm. This becomes more important if artificial light sources and lighting
2environment are involved in the process of indoor light measurement.

35) In correspondence with the results of former QUIPS analyses our data identified female
4gender, age and chronic pain and as confounders of the primary endpoint maximum pain
5regardless of the type of surgery.[20]

66) The Bonferri correction for maintaining an overall alpha-level of 0.05 was not
7implemented in our statistical analysis which could potentially raise the chance of
8false positive results.

9

10**Conclusion**

11Our data show no further evidence for light intensity-induced pain modulation in humans in
12the postoperative setting. For the secondary outcomes, the data showed an association
13between brighter light intensity and increased incidence of nausea for the first time.

14The subject should be studied under more controlled conditions concerning the variability of
15the types of surgery, hospital analgesic standards and potential strong differences between
16sunlight and artificial light concerning intensity and wavelength.

17The ideal study design would include measuring the light intensity average of a longer time
18span for a standardized sub group of patients undergoing similar or same surgical
19procedures. Furthermore, in order to have less variability, only patients from one ward with
20comparable lighting conditions and architecture should be included. Randomized controlled
21trials are needed to have further evidence for making an association between light intensity
22and acute pain intensity.

23

24

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