Using mathematical package for modeling of sleep disorders in patients with traumatic brain injury



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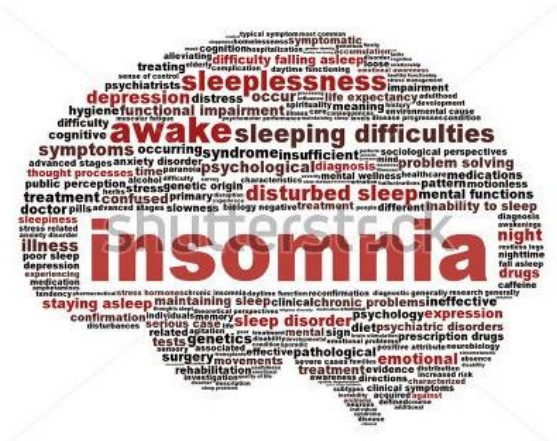
Abstract

Mathematical packages are widely used for data processing and analysis, including processing of biomedical information.

We consider the use of known mathematical packages for processing of biomedical data on patients who received a traumatic brain injury in order to determine the effect of injury severity on sleep.

The importance of the problem is related primarily to the fact that persons, who have had a traumatic brain injury, also have had sleep disturbances.

As a consequence, the quality of life and ability to work are deteriorated.



The Analysis of Biological Data

The methods and software tools for storing, retrieving, organizing and analyzing biological data are developed via bioinformatics, an interdisciplinary scientific field.

A major activity in bioinformatics is to develop software tools to generate useful biological knowledge [1].

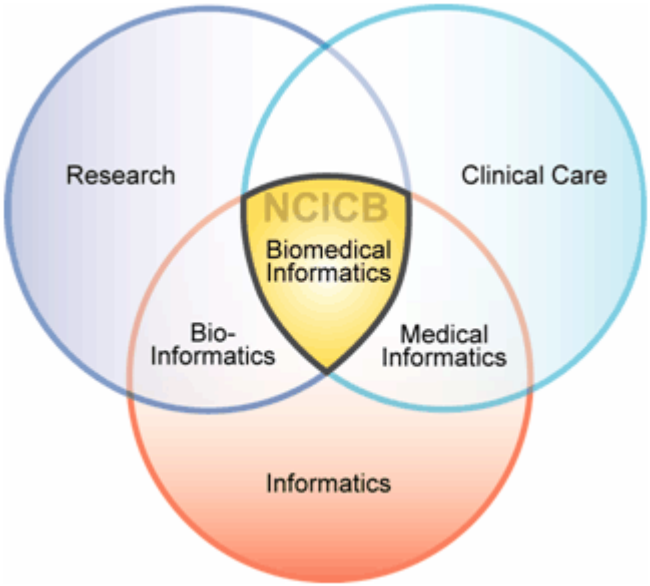
Bioinformatics combines computer science, statistics, mathematics and engineering to study biological data and processes.

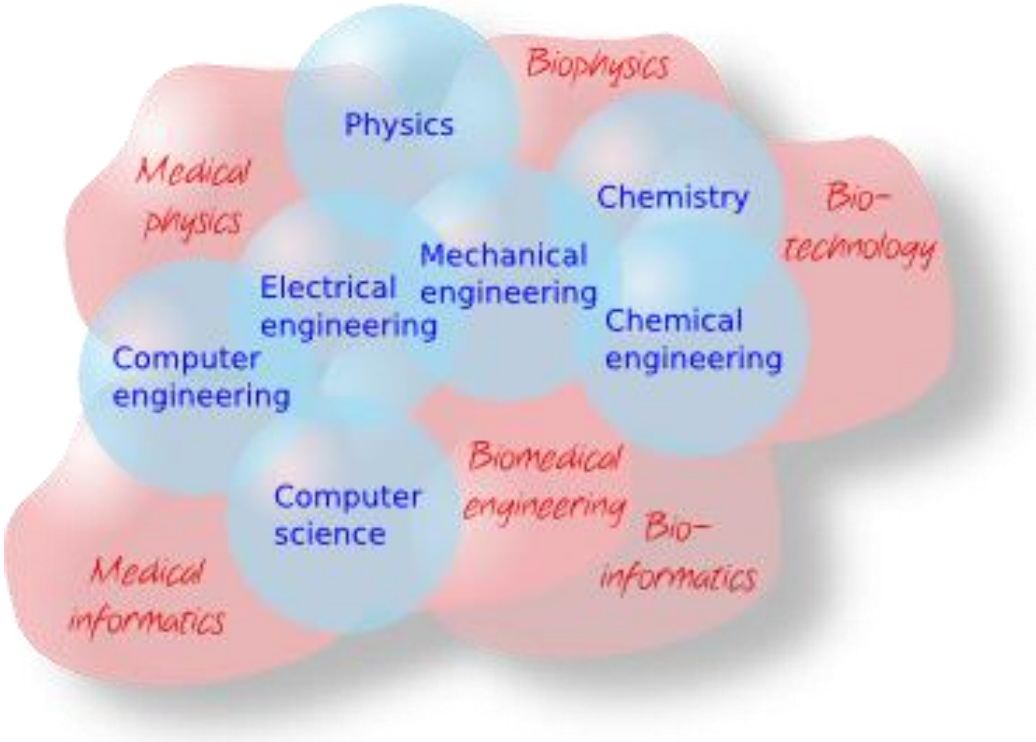
Such software tools and technologies as Java, C#, XML, Perl, C, C++, Python, R, SQL, CUDA, MATLAB, and spreadsheet applications are commonly used in the field.

[1] http://bioinformatics.com.bd/

Biomedical Informatics

In turn, the integration of bioinformatics and clinical informatics, biomedical Informatics offers unique infrastructure, tools, techniques and applications that bridge these areas. This facilitates the sharing of data and information across diverse disciplines [2].





[2] http://ncicb.nci.nih.gov/about/bioinformatics/

The Tools

So we have tools, information technologies, and analytical methodologies needed to manage the large volumes of data generated by novel types of research - and to harvest insights from the information collected.

In the research we used the R-package, Excel, and some results were obtained with using STATISTICA and Maple.

R is a free software environment for statistical computing and graphics [3].

It compiles and runs on a wide variety of UNIX platforms, Windows and MacOS.

R is highly extensible. R is designed around a true computer language, and it allows users to add additional functionality by defining new functions.

[3] http://www.r-project.org/

The Objects of Biomedical Monitoring

The original data on patients, who have had a head injury, were provided by experts from the advisory department of the Central Clinical Hospital of Kharkiv.

In order to identify sleep disorders, depending on the severity of the traumatic brain injury, the patients were divided into three groups.

The first group included 40 (40%) patients with mild craniocerebral injury .

The second group consisted of 31 (31%) patients with craniocerebral injury of moderate severity.

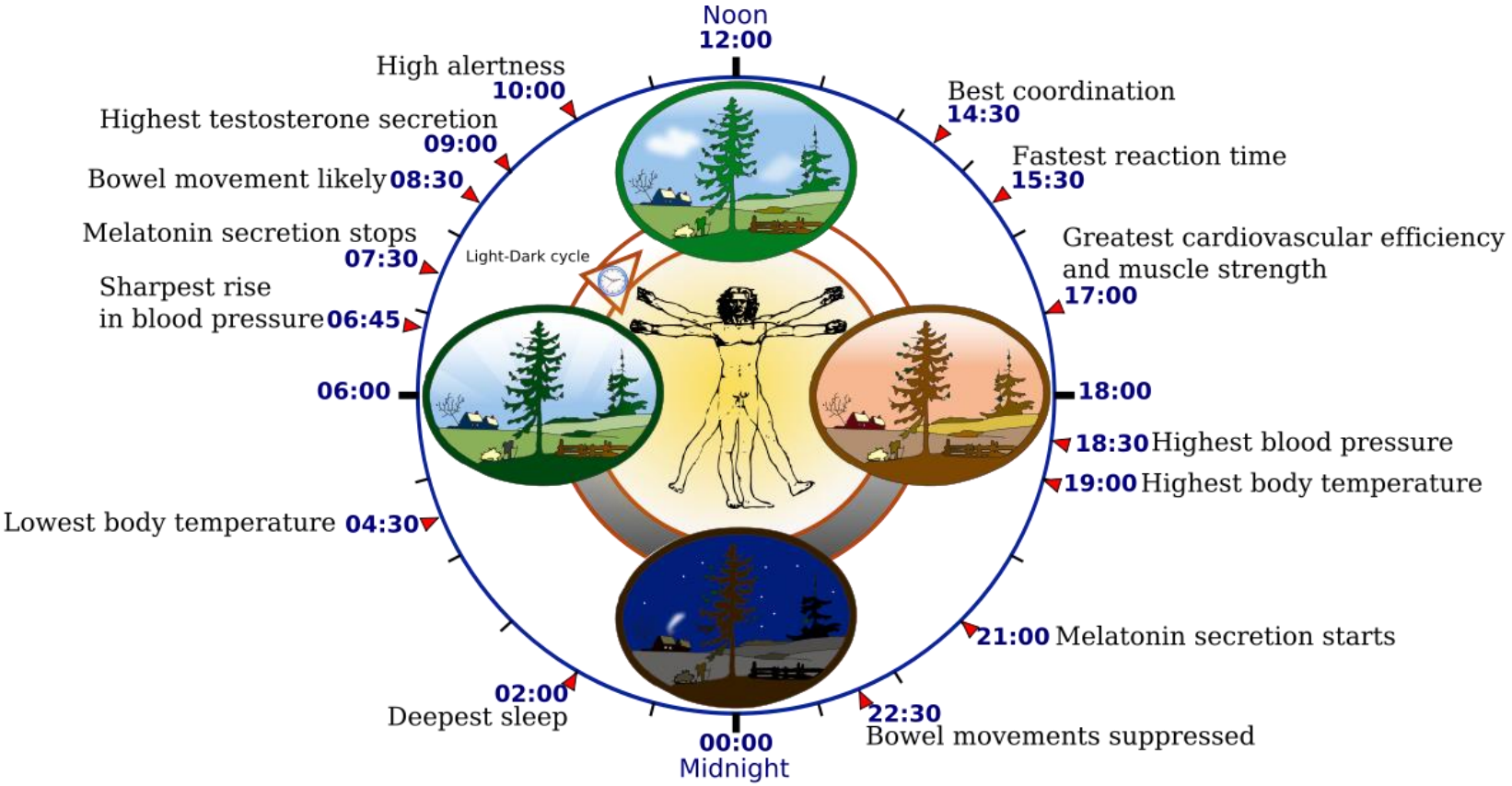
The third group included the rest - 29 (29%) patients with severe craniocerebral trauma.

All the patients had sleep disturbances.

Circadian Rhythm[4]

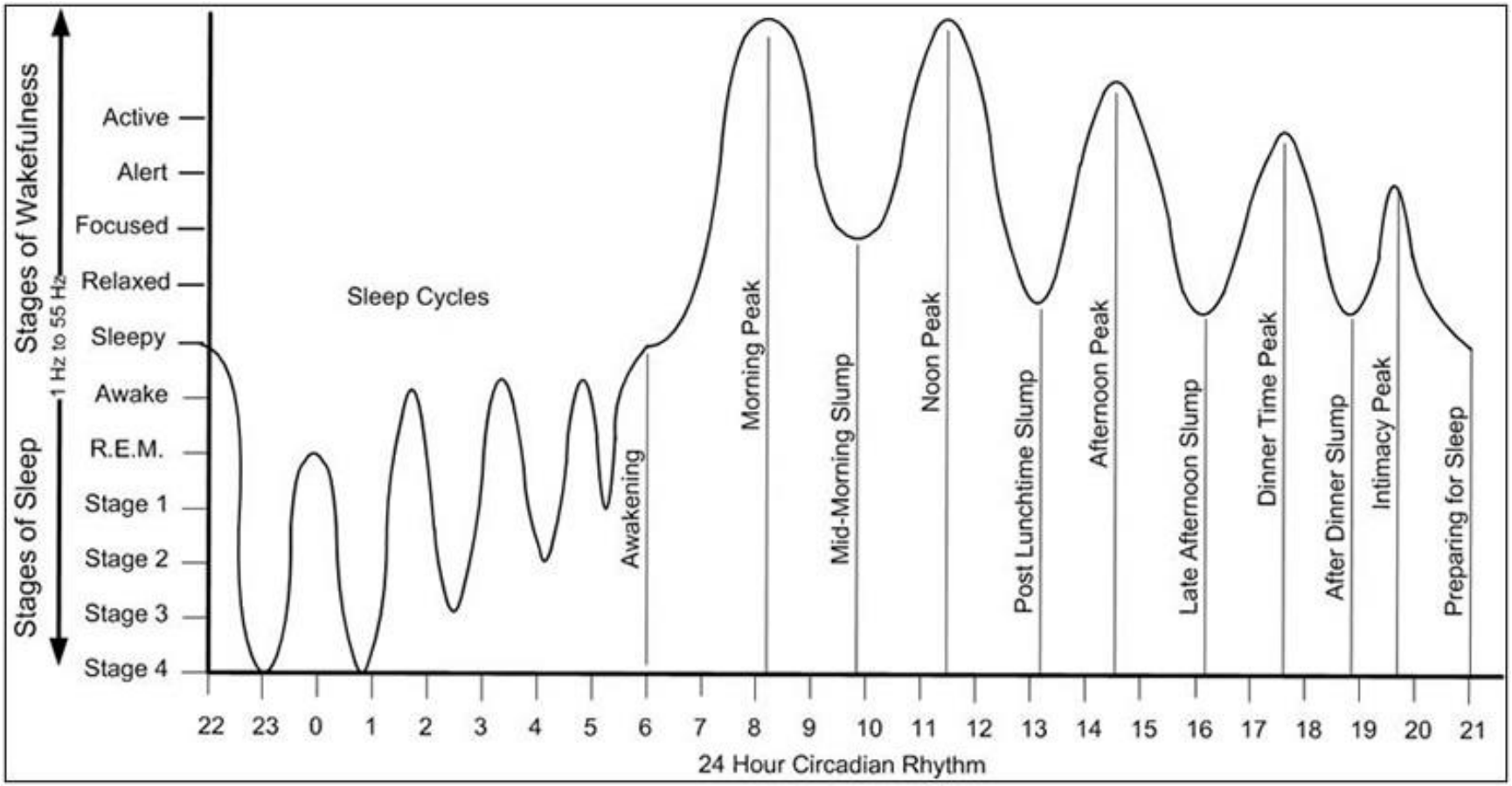
Our bodies have a repeating cycle, a rhythm lasting about (circa) a day (dian).

Just as we have multiple sleep cycles at night, we have multiple waking cycles during the day.



[4] http://en.wikipedia.org/wiki/Circadian_rhythm#mediaviewer/File:Biological_clock_human.svg

The True Rhythm of Life[5]

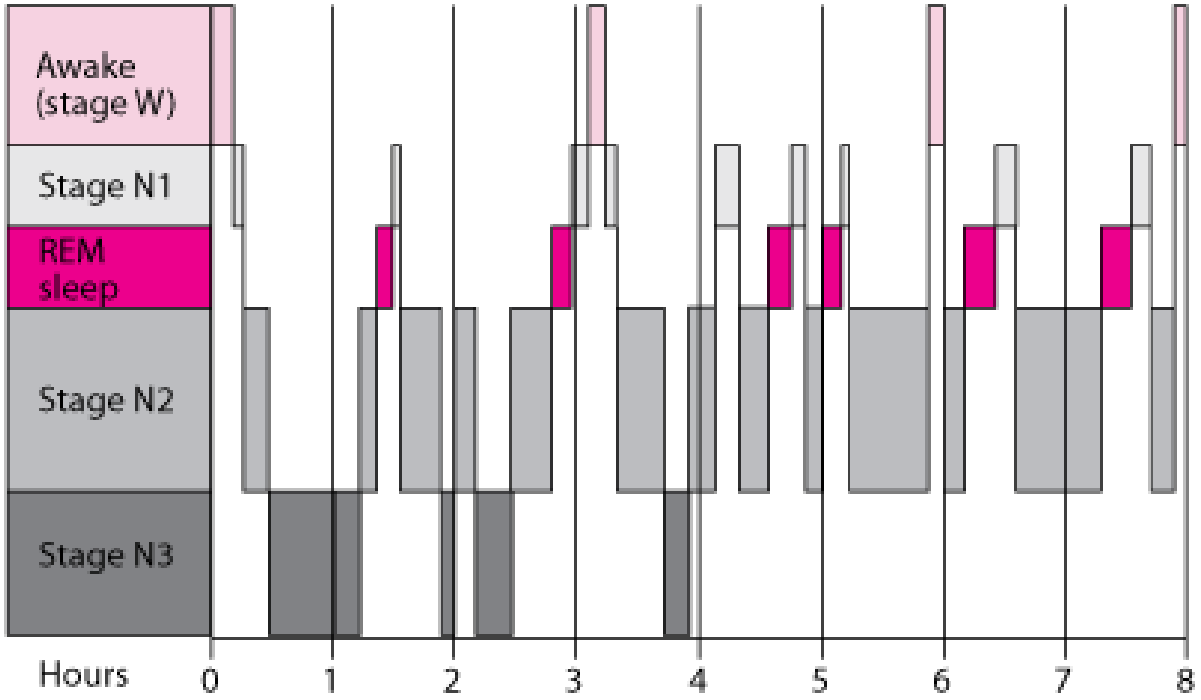


[5] The 24 Hour Circadian Rhythm [http://nutesla.com/science/circadian-rhythms/]

The types of sleep[6]

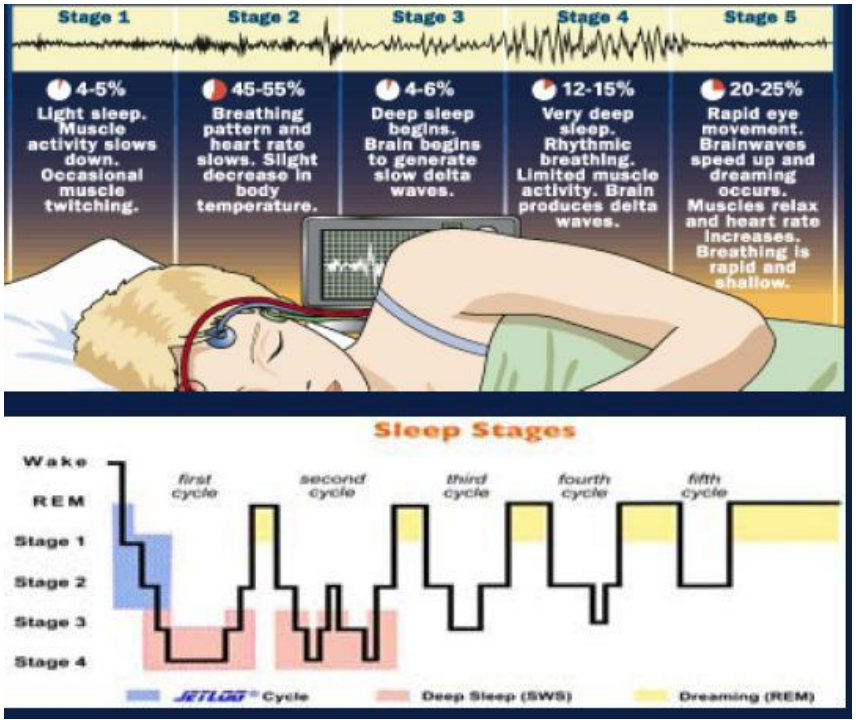
All sleep is not the same. There are two main types of sleep: rapid eye movement (REM) sleep and nonrapid eye movement (non-REM) sleep, which has three stages.

People normally cycle through the three stages of non-REM sleep (stages N1 through N3), usually followed by a brief interval of REM sleep, every 90 to 120 minutes or several times every night.



[6] http://www.merckmanuals.com/home/brain_spinal_cord_and_nerve_disorders/sleep_disorders/overview_of_sleep.html

Sleep Cycle[7] and Sleep Stages[8]



[7] Sleep cycle [http://www.examiner.com/article/unexpected-reasons-to-get-more-sleep]

[8] Sleep stages [http://craftmatic.co.nz/health-and-sleep-related-infographics/]

Sleep Disorders

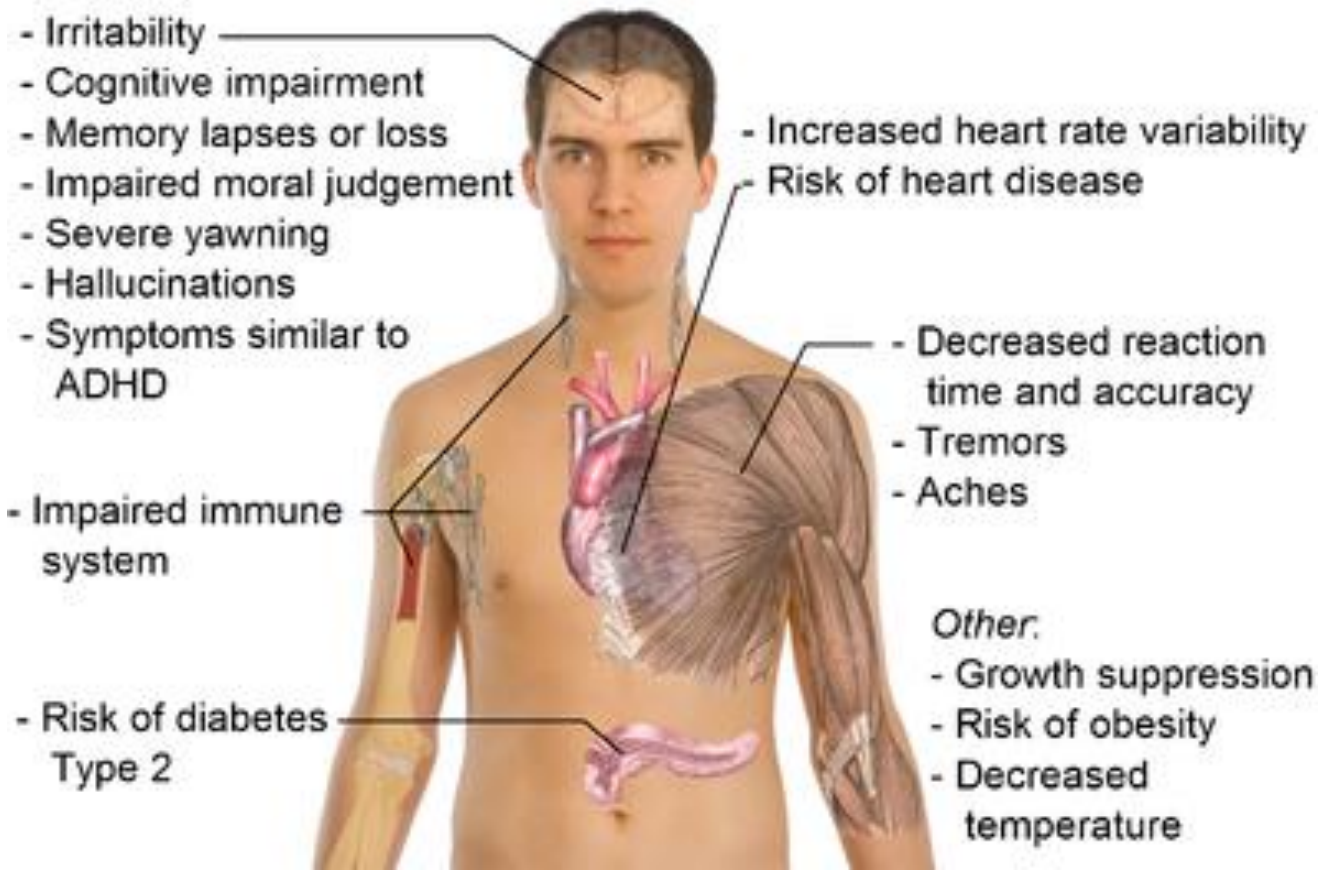
Sleep is an active and essential process that allows the body to restore itself in order to maintain cognitive and physical functioning. Unfortunately, sleep disturbances are very common all over the world.

The figure on the next slide shows the common sleeping disorders.

For each disorder, there are common symptoms associated with each disorder and available treatment measures.

Sleep specialists can diagnose them using special techniques.

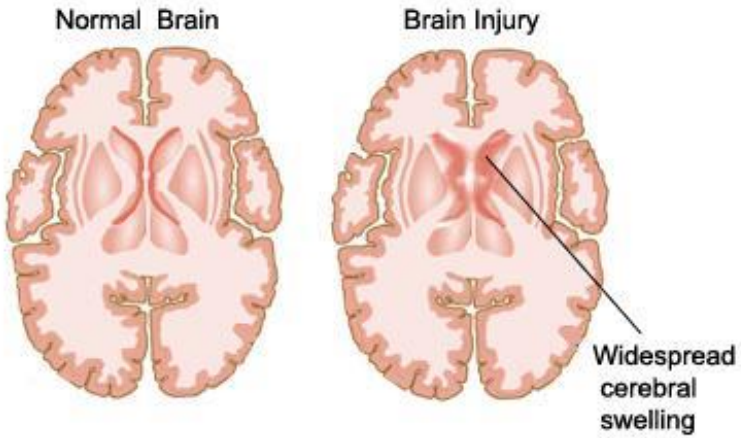
Effects of Sleep Deprivation[9]



[9] Effects of Sleep Deprivation [http://www.neurotexasinstitute.com/what-we-treat/Sleep-Disorders.aspx]

The Possible Consequences

Traumatic brain injury results from an impact to the head that disrupts normal brain function. Traumatic brain injury may affect a person's cognitive abilities, including learning and thinking skills.



The Methods of Examination

The following methods were used to survey the patients

a) an objective method of EEG night's sleep. The night sleep recording was conducted from the moment of falling asleep before waking up (4-6 hours);

b) subjective assessment of sleep and daytime sleepiness (questionnaire);

c) determining the clinical variants of sleep disorders (presomnia, intrasomnia, mixed forms and postsomnia);

d) methods of statistical analysis.

The Statistical Analysis

The descriptive statistics and other statistical methods of data analysis were applied .

The use of descriptive statistics includes the following steps:

- Data collection
- Presentation of data

Descriptive statistics uses three basic methods of data aggregation:

- Tabular presentation
- Graphic representation
- Calculation of statistical parameters

Pretreatment

Pretreatment:

- Preparation of data to statistical analysis
- Descriptive Statistics

Pretreatment consisted of the following steps:

- identifying the objects for research,
- preparation of the raw data,
- evaluation of the accuracy of the data,
- preliminary calculations,
- identifying missing data values,
- data validation,
- transferring data, received in another programs,
- preparation of secondary data.

The Statistical Processing

The performed statistical processing includes the follows:

1. Data analysis of the stages of sleep.
2. Data analysis of the stages of sleep by sex of patients.
3. Analysis of the impact of injury severity on sleep stages.
4. Analysis of the impact of injury severity on awakening within a sleep.
5. Analysis of influence of injury severity on multiple cycles of night sleep.
6. Analysis of deviations in melatonin depending on the sex of the patients.
7. Analysis of the relationship between subjective and objective measures of sleep.
8. Analysis of the relationship between objective and subjective assessments of autonomic dysfunction of sleep.
9. Constructing cluster models of sleep disorders.

The Patients

The study comprised 100 patients (75 males, mean age ± SD 38 ± 16 years, range 16–72) with acute, first-ever TBI, admitted to hospital between July 2011 and June 2012 immediately after the injury.

Patients with sleep–wake and/or psychiatric disorders diagnosed prior to TBI were excluded. The consent for study was obtained from all patients before participation (in comatose patients after regaining of the consciousness).

Preparing data for statistical analysis

The patient record consists of 19 fields.

	Field name and field designator	Data type	Data value
1	The patient number No	ordinal	from 1 to 100
2	The group number GrNo	ordi	
3	The patient number in the group PatNo	ordi	
4	The first stage X1	num	
5	The second stage X2	num	
6	The stages 3-4 X3	num	
7	REM sleep stage X4	num	
8	Objective assessment of sleep Obj	nom	
9	Subject evaluation of sleep Subj	nom	
10	Sex - Sex	nominal	м – male; ж - female
11	The chronotype Chron	nominal	г-dove; с- owl; ж- laverock
12	The period - Period	nominal	отд - remote period of injury; ост - the acute phase of injury; пром - interim period of injury
13	Age - Age	numeric	from 18 to 53 years
14	Melatonin X5	numeric	from 5.3 to 59.1
15	The position - Pos	nominal	раб-worker; рук-head
16	Vegetative-vascular dystonia, objectively - VDObj	nominal	у- moderately severe; в- denominated
17	Vegetative-vascular dystonia,, subjectively VDSubj	nominal	у- moderately severe; в- denominated
18	The shift of patient -Smena	nominal	1 or 2
19	Colour - Colour	nominal	к, г, ч, з

Table 1: The fragment of the table with initial data (Top)

No	GrNo	PatNo	X1	X2	X3	X4	Obj	Subj	Sex
1	2	3	4	5	6	7	8	9	10
1	1	1	*	26	3	0	в	у.в.	ж
2	1	2	45	83	4	3	в	у.в.	ж
3	1	3	45	*	*	*	у	у.в.	м

Table 2: The fragment of the table with initial data. (The table continuation)

No	Chron	Period	Age	X5	Pos	VDObj	VDSubj	Smena	Colour
1	11	12	13	14	15	16	17	18	19
1	г	ост	46	10,4	рук	в	в	1	ч
2	с	отд	39	14,6	раб	в	у	1	г
3	г	отд	27	40,23	раб	в	в	1	к

Table 3: The fragment of table with transformed initial data (Top)

No	GrNo	PatNo	X1	X2	X3	X4	Obj	Subj	Sex
1	2	3	4	5	6	7	8	9	10
1	1	1	0	6	-7	-5	1	0	0
2	1	2	30	63	-6	-2	1	0	0
3	1	3	30	0	0	0	0	0	1

Table 4: The fragment of table with transformed initial data (The table continuation)

No	Chron	Period	Age	X5	Pos	VDObj	VDSubj	Smena	Colour
1	11	12	13	14	15	16	17	18	19
1	1	0	46	-20,6	1	1	1	1	1
2	2	2	39	-16,4	0	1	0	1	4
3	1	2	27	-14,77	0	1	1	1	2

Fig. The initial and transformed data

Some Descriptive Statistics

The data stored in the format *. csv;

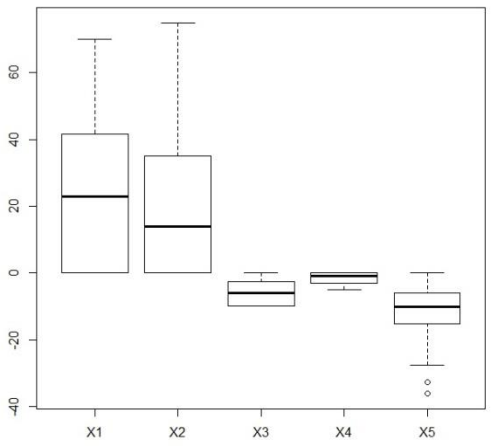
the data are processed in the R package.

```
> data<-read.csv("natanson2701.csv")
> summary(data)
       No              GrNo            PatNo             X1              X2              X3              X4              Obj             Subj
 Min.   :  1.00   Min.   :1.00   Min.   :  1.00   Min.   :  0.00   Min.   :  0.00   Min.   :-10.00   Min.   :-5.00   Min.   :0.00   Min.   :0.00
 1st Qu.: 25.75   1st Qu.:1.00   1st Qu.:  9.00   1st Qu.:  0.00   1st Qu.:  0.00   1st Qu.:-10.00   1st Qu.:-3.00   1st Qu.:0.00   1st Qu.:0.00
 Median : 50.50   Median :2.00   Median : 17.00   Median : 23.00   Median : 14.00   Median :  -6.00   Median :-1.00   Median :1.00   Median :1.00
 Mean   : 50.50   Mean   :1.89   Mean   : 17.51   Mean   : 22.12   Mean   : 19.03   Mean   :  -5.65   Mean   :-1.83   Mean   :0.54   Mean   :0.53
 3rd Qu.: 75.25   3rd Qu.:3.00   3rd Qu.: 25.25   3rd Qu.: 41.25   3rd Qu.: 35.00   3rd Qu.:  -2.75   3rd Qu.: 0.00   3rd Qu.:1.00   3rd Qu.:1.00
 Max.   :100.00   Max.   :3.00   Max.   : 40.00   Max.   : 70.00   Max.   : 75.00   Max.   :   0.00   Max.   : 0.00   Max.   :1.00   Max.   :1.00
      Sex             Chron           Period           Age              X5              Pos             VDObj           VDSubj          Smena
 Min.   :0.00   Min.   :0.00   Min.   :0.00   Min.   :18.00   Min.   :-36.20   Min.   :0.00   Min.   :0.00   Min.   :0.00   Min.   :1.00
 1st Qu.:0.00   1st Qu.:1.00   1st Qu.:1.00   1st Qu.:28.00   1st Qu.:-15.32   1st Qu.:0.00   1st Qu.:0.00   1st Qu.:0.00   1st Qu.:1.00
 Median :1.00   Median :1.00   Median :2.00   Median :36.50   Median :-10.20   Median :0.00   Median :1.00   Median :1.00   Median :1.00
 Mean   :0.64   Mean   :1.12   Mean   :1.48   Mean   :35.31   Mean   :-11.47   Mean   :0.41   Mean   :0.62   Mean   :0.71   Mean   :1.66
 3rd Qu.:1.00   3rd Qu.:2.00   3rd Qu.:2.00   3rd Qu.:42.00   3rd Qu.: -5.90   3rd Qu.:1.00   3rd Qu.:1.00   3rd Qu.:1.00   3rd Qu.:2.00
 Max.   :1.00   Max.   :2.00   Max.   :2.00   Max.   :53.00   Max.   :  0.00   Max.   :1.00   Max.   :1.00   Max.   :1.00   Max.   :3.00
```

> data1<-data[,c(4,5,6,7,14)]

> snat1 <- stack(data1)

> boxplot(snat1$values ~ snat1$ind)



DATA OF THE MULTIFACTOR MODEL OF SLEEP DISORDERS

The Correlation Matrix

	GrNo	X1	X2	X3	X4	Obj	Sex	Chron	Period	Age	X5	Pos	VDObj	Smena	Colour
GrNo	1.000	-0.138	-0.3454	0.325	0.422	-0.050	0.3300	0.0769	0.189	-0.179	0.531	0.0126	0.046	0.047	0.3344
X1	-0.138	1.000	0.0997	-0.064	-0.053	0.146	-0.0178	-0.1419	0.115	0.202	-0.157	-0.0132	-0.145	0.038	0.3737
X2	-0.345	0.100	1.0000	-0.409	-0.269	0.269	-0.0676	-0.0471	0.027	0.120	-0.315	-0.0022	-0.070	-0.038	-0.1243
X3	0.325	-0.064	-0.4089	1.000	0.458	-0.384	0.1403	-0.1613	0.023	-0.139	0.489	0.0927	0.041	-0.036	0.0518
X4	0.422	-0.053	-0.2692	0.458	1.000	-0.361	0.2500	-0.1388	0.040	-0.243	0.426	0.1116	0.138	0.105	0.2466
Obj	-0.050	0.146	0.2686	-0.384	-0.361	1.000	-0.1070	0.0447	-0.022	0.141	-0.536	-0.0465	-0.061	-0.087	0.0695
Sex	0.330	-0.018	-0.0676	0.140	0.250	-0.107	1.0000	-0.1429	0.178	-0.266	0.150	-0.0102	-0.115	0.019	-0.0073
Chron	0.077	-0.142	-0.0471	-0.161	-0.139	0.045	-0.1429	1.0000	-0.013	-0.115	0.090	0.0024	0.047	-0.103	-0.0628
Period	0.189	0.115	0.0266	0.023	0.040	-0.022	0.1776	-0.0130	1.000	0.057	0.080	0.0314	0.054	-0.051	0.0484
Age	-0.179	0.202	0.1201	-0.139	-0.243	0.141	-0.2657	-0.1155	0.057	1.000	-0.073	0.0696	0.114	0.096	0.0830
X5	0.531	-0.157	-0.3150	0.489	0.426	-0.536	0.1496	0.0896	0.080	-0.073	1.000	0.0489	0.045	0.045	0.1062
Pos	0.013	-0.013	-0.0022	0.093	0.112	-0.047	-0.0102	0.0024	0.031	0.070	0.049	1.0000	0.066	-0.098	-0.0018
VDObj	0.046	-0.145	-0.0697	0.041	0.138	-0.061	-0.1150	0.0471	0.054	0.114	0.045	0.0662	1.000	0.002	0.1838
Smena	0.047	0.038	-0.0375	-0.036	0.105	-0.087	0.0189	-0.1034	-0.051	0.096	0.045	-0.0984	0.002	1.000	0.0951
Colour	0.334	0.374	-0.1243	0.052	0.247	0.069	-0.0073	-0.0628	0.048	0.083	0.106	-0.0018	0.184	0.095	1.0000

The matrices of factor loadings

- before rotation

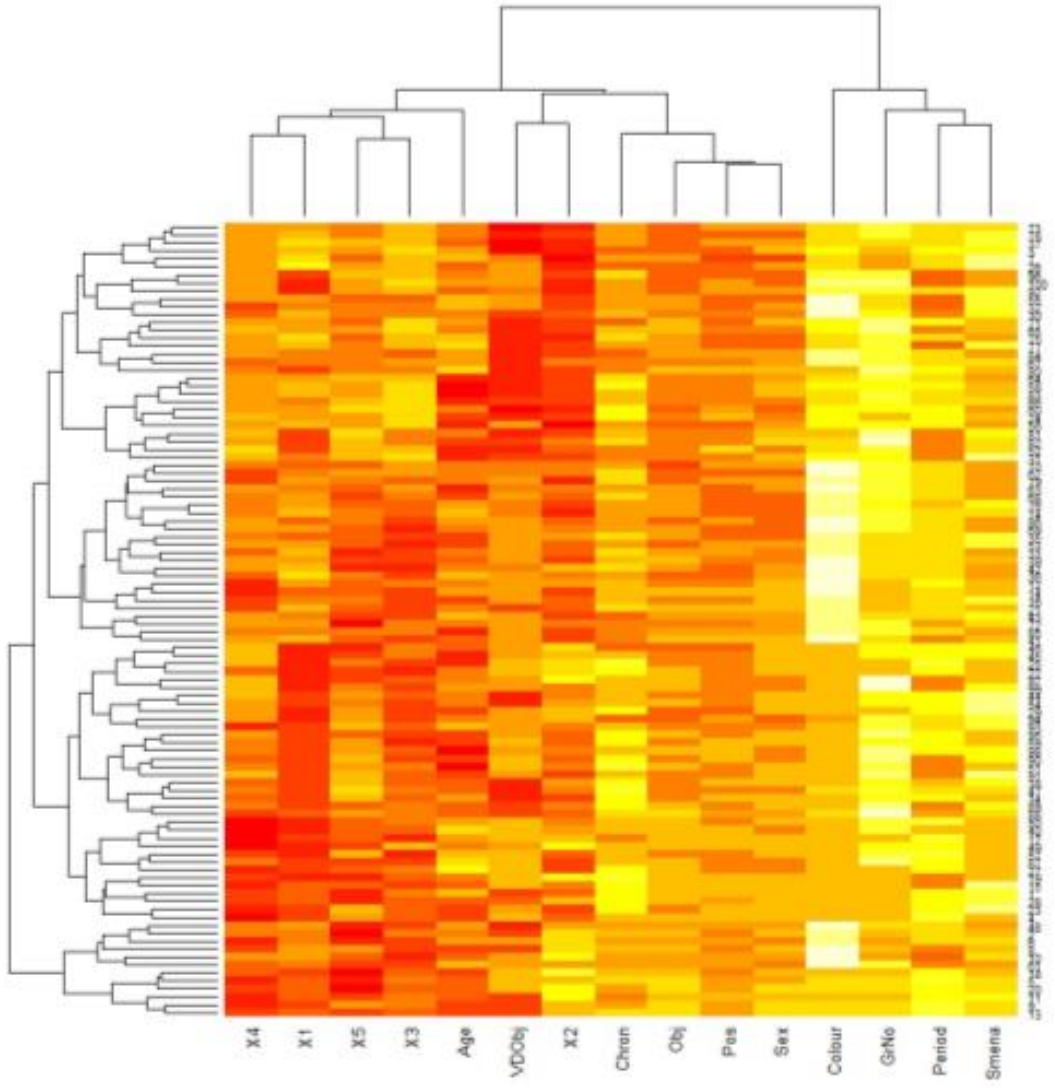
	PC1	PC2	PC3	PC4	PC5	PC6	PC7	PC8	PC9	PC10	PC11	PC12	PC13	PC14	PC15
[1,]	23.46999	-0.9574165	-13.77180	10.276375	-0.307626	2.0449660	-0.0432406	0.8679449	-1.0719775	0.1756206	0.19220986	-0.618222	0.37647745	-0.1459793	0.08207799
[2,]	-26.47692	36.1489896	-0.5347927	-2.827943	-2.485373	-0.832648	1.68742941	-0.383503	-0.7556220	-0.655762	-1.1878932	0.6531274	-0.0347370	-0.2083516	0.29792463
[3,]	1.893407	-20.695102	8.0835942	3.306234	-4.932138	0.0571433	-0.7937008	-0.497368	-0.3471154	0.3097999	-0.9984481	0.5684320	0.11273393	0.4942524	0.15342931
[4,]	-6.205860	-11.492741	14.5711800	24.987717	-2.689623	2.3094779	-0.0698786	-1.026063	0.2074505	-0.787609	-0.0735582	0.3347164	-0.4715278	0.3975484	-0,1781198
[5,]	-20.06274	10.8059194	-0.1700766	9.225318	-1.839338	2.4154065	-0.3424351	0.9591766	-0.9301141	-0.151351	0.59740350	-0.624601	-0.1918747	-0.4062511	-0.2974937
[6,]	-29.20672	26.4147732	18.9095766	7.959729	1.1868030	1.2505528	2.48477537	0.1335141	0.8106988	0.4300771	-0.7239603	0.2024756	-0.4520403	-0.6670489	-0.1174355

- after rotation

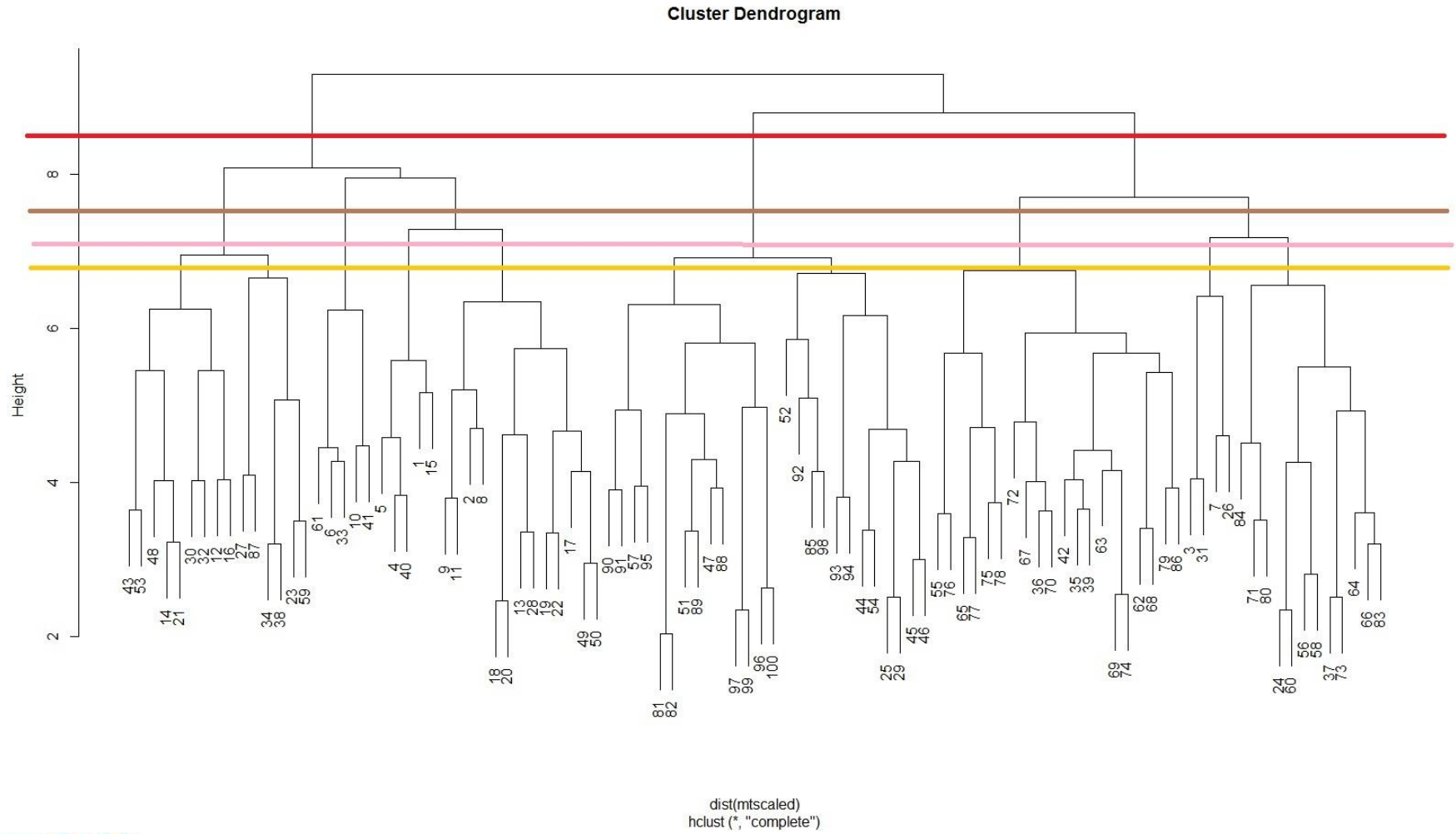
	PC1	PC2	PC3	PC4	PC5	PC6	PC7	PC8	PC9	PC10	PC11	PC12	PC13	PC14	PC15
GrNo [1,]	0.00956701	-0.0108024	0.01227665	-0.048130	0.00749005	-0.1251177	0.21653963	-0.2577808	0.14646397	-0.3000864	0.71671899	-0.0678222	0.21754373	-0.0910167	-0.4276341
X1 [2,]	-0.8942069	-0.4367475	0.08637224	-0.0380439	0.0097939	0.01252400	-0.0193455	0.00112934	-0.0018563	-0.0055992	0.00387777	-0.0011925	0.00718542	0.00035721	-0.0026195
X2 [3,]	-0.4248658	0.89196811	0.05911437	-0.1354258	-0.0435941	-0.0053892	0.0085750	0.00149152	0.0009567	-0.0045843	0.00198361	0.0006407	0.00091295	0.00080254	-0.0037805
X3 [4,]	0.03639468	-0.0656105	0.04537713	-0.2226467	-0.9449697	0.19372665	0.09231892	0.01040714	0.02412544	-0.0505561	-0.0142273	0.01037945	-0.0059891	0.00459352	0.01029882
X4 [5,]	0.01465287	-0.0236199	0.05376928	-0.1064288	-0.1870211	-0.8902344	-0.3674420	-0.0188203	-0.1046788	-0.0559255	-0.0289398	0.05344292	-0.0323897	-0.0446814	0.03636787
Obj [6,]	-0.0053095	0.00474789	-0.0056902	0.03166788	0.01132767	0.00598496	0.09524851	-0.0642878	-0.0225821	-0.1595943	0.30044267	-0.0115651	0.13569912	-0.3791454	0.84083256

THE CLUSTER MODEL OF SLEEP

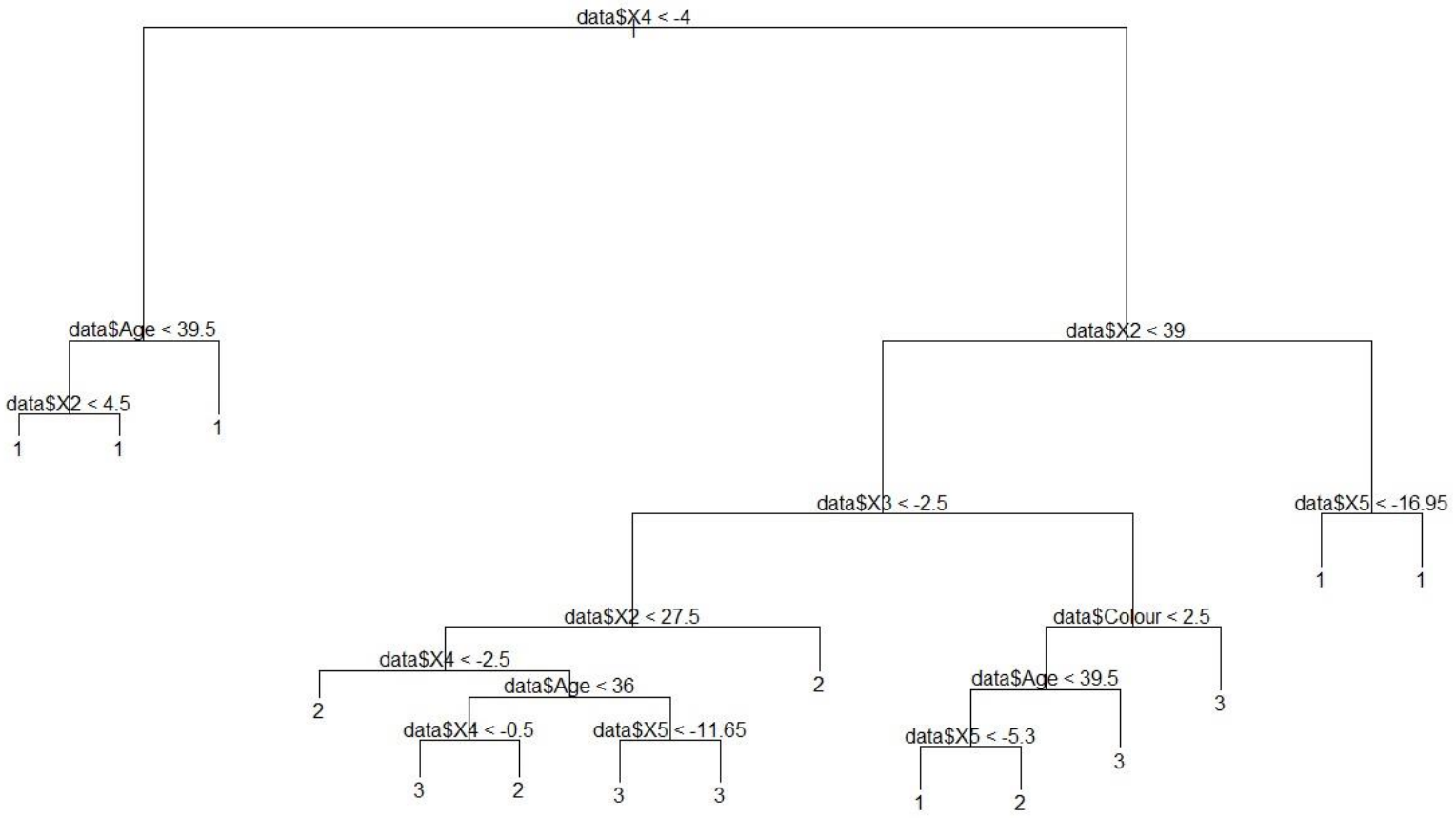
The Heat Map


X4
X1
X5
X3
Age
VDObj
X2
Chron
Obj
Pos
Sex
Colour
GrNo
Period
Smena

The Hierarchical Tree



The Classification Tree



The Findings -1

The analysis of the results of statistical processing by using R package allowed to draw conclusions that:

- With increasing number of groups (severity of injury) deviations from the norm, i.e., violations of sleep stages are reduced.
- For the third stage of sleep is marked the highest percentage of patients with deficiencies in groups 1 and 2, this percentage has the greatest value.
- Violation of the 1st and 2nd stages of sleep have positive deviations from the norm, and stage 3-4 and REM sleep - negative deviations.
- Gender has no significant effect on the violation of the sleep stages.
- For both sexes the decrease abnormal disturbances of sleep stages with increasing numbers of the group were confirmed. And the deviation in women decreased slightly faster than that of men (with the exception of sleep stages 3-4).

The Findings -2

- Hypothesis about the influence of gender on violations of sleep stages was not confirmed.

- The analysis confirmed the hypothesis about the influence of the severity of injury to the violation of sleep stages 2, 3-4, and REM sleep. The strongest effect is in the stage of REM sleep. There was no effect on the stage 1.

- The extent of the injury affects the awakening within a dream. It is noted an inverse relationship: with increasing severity of injury the awakening within a dream decreases.

- The extent of the injury has little effect on the multiplicity of violations cycles night's sleep. However, we can note a slight decrease in violations multiplicity night sleep cycles with increasing degree of injury.

- The analysis of melatonin deviations between patients of both sexes in the three groups confirmed: there are no differences according to gender; there are significant differences between groups 1, 2 and 3 for the same sex.

The Findings -3

As a result of multivariate analysis using principal component analysis identified the most significant signs of sleep disorders, they are:

- the variables X2, X3, X4, X5 and Obj, i.e. deviation of the duration of a 2, 3-4, and REM sleep from the norm, as well as deviations from the norm of melatonin and objective assessment of sleep;
- the variables X1, Colour, Age and Chron, i.e. deviation of the duration of the 1st stage of sleep from the norm, sleep disorders, age and chronotype;
- other features are not meaningful indicators.

Use of the classification tree allows with a certain degree of certainty to identify the severity of injury to such data as:

- Violations of stage REM sleep (X4);
- Disorders of steps 2 and 3-4 sleep (X2 and X3);
- The amount of melatonin (X5);
- Age (Age);
- Mixed and other sleep disorders (Colour).

The List of References

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THANK YOU FOR ATTENTION!