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Motor and emotional behavior in experimentally induced depression

Comportamentul motor şi emoţional în depresia indusă experimental

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Abstract

Background. Sleep changes are frequently associated with type 2 diabetes mellitus, obesity and arterial hypertension, and are correlated with major depressive and metabolic disorders.

Aims. We aimed to experimentally study in non-obese and obese female rats the following: depression induced by moderate chronic stress, sleep deprivation, olfactory bulbectomy; the influence of obesity on depression by sleep deprivation; changes in motor and emotional behavior in animals with depression.

Methods. The research was performed in 4 groups (n=10 animals/group), as follows: group I – control group; group II – with depression by sleep deprivation, induced by sound stimuli; group III – female rats with depression induced by olfactory bulbectomy; group IV – female rats with obesity (by administration of 3 ml fat/day by oropharyngeal gavage; the fat lipid content was 93%), and depression by sleep deprivation. Depression by sleep deprivation was induced by exposure for 120 minutes/24 hours (5 minutes/hour, respectively) to a continuous sound stimulus automatically generated by a bell: 5 dB - original model) and using the Kelly method by bilateral olfactory bulbectomy. Involuntary motility was tested using the open field test. The examination moments were: day 1 and day 28. Statistical processing was performed using the Excel application (Microsoft Office 2007) and the StatsDirect v. 2.7.2. program.

Results. The open field test values - emotional score, taking into consideration all groups, evidenced very statistically significant differences between at least two groups, both at moment T_0 (p=0.0078) and at moment T_{28} (p=0.0049). The open field test values - motility score, taking into consideration all groups, showed highly statistically significant differences between at least two groups, both at moment T_0 and at moment T_{28} (p<0.0001).

Conclusions. Emotional behavior decreases after depression induced by sleep deprivation and olfactory bulbectomy, compared to controls. Involuntary motor behavior increases in all groups with depression, compared to initial values.

Key words: depression, Open Field test.

Rezumat

Premize. Modificările de somn sunt asociate frecvent cu diabetul zaharat de tip 2, obezitatea şi hipertensiunea arterială şi se corelează cu tulburările depresive majore şi cu cele metabolice.

Obiective. Ne-am propus să studiem experimental pe animale, şobolani femele, neobeze şi obeze: depresia indusă prin stres moderat cronic, prin deprivare de somn, bulbectomie olfactivă; influenţa obezităţii asupra depresiei, prin deprivare de somn; modificările comportamentului motor şi emoţional la animale cu depresie.

Metode. Cercetările au fost efectuate pe 4 loturi (n=10 animale/lot), după cum urmează: Lot I – martor control; Lot II – cu depresie prin deprivare de somn, indusă prin stimuli sonori; Lot III – femele cu depresie indusă prin bulbectomie olfactivă; Lot IV – femele cu obezitate (prin administrare de 3 ml de untură/zi prin gavaj orofaringian; conţinutul lipidic al unturii a fost de 93%) şi depresie, prin deprivare de somn. Depresia prin deprivare a fost indusă prin: expunerea timp de 120 minute/24 ore (respectiv 5 minute/oră) la un stimul sonor continuu generat automat de o sonerie: 5 dB - model original) şi metoda Kelly, prin bulbectomie olfactivă bilaterală. Testarea motilităţii involuntare s-a făcut prin Testul Open Field. Momentele pentru examinare au fost: ziua 1 şi ziua 28. Prelucrarea statistică s-a efectuat cu aplicaţia Excel (din pachetul Microsoft Office 2007) şi cu programul StatsDirect v.2.7.2.

Rezultate. Testul Open Field - scor emotivitate, luând în considerare toate loturile, au fost observate diferenţe statistic foarte semnificative între cel puţin două loturi, atât la momentul T_0 (p=0,0078), cât şi la momentul T_{28} (p=0,0049). Testul Open Field - scor motilitate, luând în considerare toate loturile, au fost observate diferenţe statistic intens semnificative între cel puţin două dintre loturi, atât la momentul T_0, cât şi la momentul T_{28} (p<0,0001).

Concluzii. Comportamentul emoţional scade după depresia indusă prin deprivare de somn şi bulbectomie olfactivă, faţă de martori. Comportamentul motor involuntar creşte la toate loturile cu depresie, faţă de valorile iniţiale.

Cuvinte cheie: depresie, testul Open Field.

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Introduction

Depression is a multicausal affective disorder, characterized by mood changes, sleep disorders, alterations of daily routine activity, changes in social behavior, appetite changes. Major depressive disorder (MDD) – mono- or unipolar disorder - may take several forms: major depressive disorder with psychotic factors, melancholy, atypical depression, postpartum depression, recurrent depression, treatment resistant depression, seasonal depressive disorder, and depressive disorder with catatonic factors (Prelipceanu, 2011).

In human pathology, obesity is considered a risk factor in the development of depression (Berk et al., 2013), but at the same time, it can be a comorbidity associated with depression (Kudlow et al., 2013).

Sleep changes (insomnia/hypersomnia) are frequently associated with type 2 diabetes mellitus, obesity and arterial hypertension, and are correlated with major depressive and metabolic disorders (Kudlow et al., 2013).

Objectives

We aimed to experimentally study in non-obese and obese female rats the following:

a) Depression induced by moderate chronic stress, sleep deprivation, olfactory bulbectomy;

b) The influence of obesity on depression by sleep deprivation;

c) Changes in motor and emotional behavior in animals with depression.

Hypothesis

Depression studied over the past fifty years in genetic animal or induced depression models is associated with locomotor, emotional, motor learning and memory changes.

Changes of locomotor and emotional behavior and of motor learning capacity have been studied particularly in animals with depression experimentally induced by bilateral olfactory bulbectomy (Takahashi et al., 2011; Romeas et al., 2009; Gao et al., 2009; Roche et al., 2008; Mchedlidze et al., 2011).

The depression - obesity - sleep disorders association led us to study in obese animals with experimentally induced depression the changes of motor and emotional behavior.

Material and methods

Research protocol

a) *Period and place of the research*

The research was performed in Wistar female rats aged 4 months, with a mean initial weight of 160 g, from the Biobase of the ”Iuliu Haţieganu” University of Medicine and Pharmacy Cluj-Napoca. The study was carried out in the Experimental Research Laboratory of the Department of Physiology, with the approval of the Bioethics Board, in the period 1.10.2013-15.11.2013.

The animals were maintained under adequate *vivarium* conditions: constant temperature (20-23ºC); humidity 35-45%; light/dark cycle (12 h light, from 8 a.m. / 12 h dark); standard feeding (combined grain feed, Cantacuzino Institute, Bucharest); water *ad libitum*. All procedures were in accordance with Directive 86/609/EEC of 24 November 1986, regarding the protection of animals used for experimental and scientific purposes.

Subjects and groups

Groups

The research was performed in 4 groups (n=10 animals/ group), as follows:

group I –control group;

group II – with depression by sleep deprivation, induced by sound stimuli;

group III – female rats with depression induced by olfactory bulbectomy (Kelly method);

group IV – female rats with obesity (by administration of 3 ml fat/day by oropharyngeal gavage; the fat lipid content was 93%), and depression by sleep deprivation.

The mean weight of the animals was 159.4 g for groups I, II and III and 307 g for group IV on day 28.

b) *Tests applied*

- Depression was induced by exposure for 120 minutes/24 hours (5 minutes/hour, respectively) to a continuous sound stimulus automatically generated by a bell: 5 dB - original model) and using the Kelly method by bilateral olfactory bulbectomy (Kelly et al., 1997).

- Involuntary motility was tested using the open field test (OFT), according to Denenberg & Whimby (1963). The monitored indicators were emotivity and motility. Emotivity was calculated based on the emotional score (ES): the sum of micturitions and defecations expressed in absolute values. The increase of their number is considered an indicator of anxiety. Spontaneous motility was calculated based on the motility score (MS): the sum of crossings and rearings. The increase of motility is and indicator of the absence of anxiety.

The examination moments were: T_1 (day 1) and T_{28} (day 28).

At the end of the experiment, the animals were euthanized with ketamine in a dose of 0.2 ml/100 g animal.

c) Statistical processing

Statistical analysis

Statistical processing was performed using the Excel application (Microsoft Office 2007) and the StatsDirect v.2.7.2. program.

Results

The statistical analysis of the *open field test values - emotional score, taking into consideration all groups*, evidenced very statistically significant differences between at least two groups both at moment T_0 ($p = 0.0078$) and at moment T_{28} ($p = 0.0049$).

The statistical analysis of the *open field test values - motility score*, *taking into consideration all groups,* showed highly statistically significant differences between at least two groups, both at moment T_0 and at moment T_{28} ($p < 0.0001$).

a) *Analysis by moments* (Table I)

The statistical analysis of the *open field test values for unpaired samples* revealed the following:

- for the emotional score

o at moment T_0 - very statistically significant differences between groups I-II ($p < 0.01$) and statistically significant differences between groups II-IV ($p < 0.05$)

Table I

Comparative analysis for open field test values and statistical significance.

Group	OPEN FIELD test		Mean	SE	Median	SD	Min.	Max.	Statistical significance (p) Unpaired samples		
									Groups I – II	Groups I – III	Groups I – IV
I	Emotional score	T_0	9.20	0.7424	10	2.3476	5	12	0.0041	0.0505	0.1027
		T_{28}							0.007	0.0264	0.1911
	Motility score	T_0	20.10	0.6904	20	2.1833	17	23	0.9917	< 0.0001	< 0.0001
		T_{28}							0.0015	< 0.0001	< 0.0001
									Groups II – III	Groups II – IV	Groups III – IV
II	Emotional score	T_0	5.80	0.6110	6.50	1.9322	3	8	0.0502	0.023	0.482
		T_{28}	6.20	0.5538	5.50	1.7512	4	9	0.1581	0.0116	0.028
	Motility score	T_0	20.00	0.6146	19.50	1.9437	17	23	< 0.0001	< 0.0001	< 0.0001
		T_{28}	24.00	0.6325	24.00	2.0000	21	27	< 0.0001	< 0.0001	< 0.0001
Group	OPEN FIELD test		Mean	SE	Median	SD	Min.	Max.	Statistical significance (p) Paired samples (T_1-T_{28})		
									Group I	Group II	Group III
III	Emotional score	T_0	7.40	0.2211	7.50	0.6992	6	8	—	0.7422	0.4609
		T_{28}	7.00	0.2981	7.00	0.9428	6	9			
	Motility score	T_0	6.80	0.4163	7.00	1.3166	5	8	—	0.0039	0.1289
		T_{28}	7.60	0.3399	7.00	1.0750	7	10			
									Group IV		
IV	Emotional score	T_0	7.80	0.3590	7.50	1.1353	6	9	0.3750		
		T_{28}	8.20	0.3266	8.50	1.0328	6	9			
	Motility score	T_0	11.40	0.4522	11.00	1.4298	10	14	0.002		
		T_{28}	14.60	0.3399	15.00	1.0750	13	16			

○ at moment T_{28} - very statistically significant differences between groups I-II ($p < 0.01$) and statistically significant differences between groups I-III, II-IV and III-IV ($p < 0.05$)

- for the motility score

○ at moment T_0 - highly statistically significant differences between groups I-III, I-IV, II-III and II-IV ($p < 0.001$)

○ at moment T_{28} - very statistically significant differences between groups I-II ($p < 0.01$) and highly statistically significant differences between groups I-III, I-IV, II-III, II-IV and III-IV ($p < 0.001$).

b) *Analysis by groups* (Table I)

The statistical analysis of the *open field test values for paired samples (T_0-T_{28})* evidenced for:

- the emotional score - highly statistically significant differences for group I ($p < 0.001$)

- the motility score - highly statistically significant differences for group I ($p < 0.001$) and very statistically significant differences for groups II and IV ($p < 0.01$).

c) *Correlation analysis of scores by groups and moments* (Table II)

Table II

Statistical correlation analysis between the open field test scores in the four groups.

Group	Moment	Emotional score – Motility score	
I	T_0	-0.1250	*
	T_{28}	-0.1250	*
II	T_0	0.6050	***
	T_{28}	-0.6669	***
III	T_0	0.4401	**
	T_{28}	-0.2662	**
IV	T_0	-0.1526	*
	T_{28}	-0.4235	**

For *group I*, the statistical correlation analysis between the values of the studied indicators showed:

- at moment T_0 – a weak/null correlation between the emotional score and the motility score

- at moment T_{28} – a weak/null correlation between the emotional score and the motility score.

For *group II*, the statistical correlation analysis between the values of the studied indicators showed:

- at moment T_0 – a good positive correlation between the emotional score and the motility score

- at moment T_{28} – a good negative correlation between the emotional score and the motility score.

For *group III*, the statistical correlation analysis between the values of the studied indicators showed:

- at moment T_0 – an acceptable positive correlation between the emotional score and the motility score

- at moment T_{28} – an acceptable negative correlation between the emotional score and the motility score.

For *group IV*, the statistical correlation analysis between the values of the studied indicators showed:

- at moment T_0 – a weak/null correlation between the emotional score and the motility score

- at moment T_{28} – an acceptable negative correlation between the emotional score and the motility score.

Discussions

Our research was performed on female rats, given the disease prevalence of 25% for women and 12% for men (Prelipceanu 2011).

Our results for OFT show that depression induced by sleep deprivation (G II) determines at 28 days, compared to controls (G I), significant decreases of ES and significant increases of MS, with a good negative correlation between the scores.

Depression induced by olfactory bulbectomy (G III) determines at 28 days, compared to controls (G I), significant decreases of ES and MS, with an acceptable negative correlation between the scores. Compared to the group in which depression was induced by sleep deprivation (G II), significant decreases of MS were found.

In obese animals, in which depression was induced by sleep deprivation (G IV), at 28 days, there were significant decreases of MS compared to controls (G I), significant increases of ES and significant decreases of MS compared

to non-obese animals with depression induced by sleep deprivation (G II), and significant increases of ES and MS compared to animals with depression induced by olfactory bulbectomy (G III). In group IV, there was an acceptable negative correlation between ES and MS.

Compared to initial values (moment T_0), at 28 days (moment T_{28}), there were significant increases of ES in G II and G IV and significant decreases of ES in G III. The motility score increased significantly at 28 days in groups II and IV, with the highest increases in G II.

The comparative analysis of the two induced depression models (G II and G III) only showed changes in MS, which significantly decreased in G III, at moments T_0 and T_{28}.

Obesity in animals with depression (G IV), compared to controls (G II), caused changes in ES, which significantly increased at moments T_0 and T_{28}, and in MS, which significantly decreased at moments T_0 and T_{28}.

Our data showed a diminution of locomotor activity: involuntary motility and exploratory behavior in animals with depression induced by olfactory bulbectomy, compared to animals with depression by sleep deprivation. In obese animals with experimentally induced depression, there was a diminution of locomotor activity: involuntary motility and exploratory behavior compared to non-obese depressive control animals.

Our results are in accordance with the data of other authors regarding the decrease of locomotor and exploratory behavior and the increase of immobility in animals with induced depression (Che et al., 2013; Tasset et al., 2010; Husain et al., 2011; Shaw et al., 2009; Wang et al., 2009; Romeas et al., 2009).

Moderate chronic stress by sound stimuli, used by us for inducing depression, is a valid model that supports its association with depression, as a form of stress by overstraining, which elicits characteristic locomotor and emotional behavioral responses (Derevenco et al., 1992; Riga & Riga 2008; Prelipceanu, 2011).

Physical exercise has favorable anti-depressive effects on locomotor activity in depression (Bruja, 2014; Che et al., 2013; Hendriksen et al., 2012; Shaw et al., 2009; Wang et al., 2009; Romeas et al., 2009; Roche et al., 2008) and is recommended as a form of therapy in depression.

Conclusions

1. Emotional behavior decreases after depression induced by sleep deprivation and olfactory bulbectomy, compared to controls.

2. Involuntary motor behavior increases after depression induced by sleep deprivation and decreases after depression induced by olfactory bulbectomy and in obese animals with depression induced by sleep deprivation, compared to controls.

3. Involuntary motor behavior increases in all groups with depression, compared to initial values.

Conflicts of interests

There are no conflicts of interest.

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