Effect of female sex hormones on hypothalamic blood flow and CO$_2$-sensitivity of hypothalamic vessels and global cerebral blood volume

PhD thesis

Emese Szelke MD

Semmelweis University
Doctoral School of Basic Medicine
Institute of Human Physiology and Clinical Experimental Research

Tutor: Peter Sándor, MD, PhD DMSc.
Szabolcs Varbiro MD, PhD

Budapest, 2010
Introduction

In the developed countries of the world the life expectancy is better, and these changes mean a big challenge for health systems. The incidence and mortality of cardiovascular diseases increase in elderly. Data from the literature show that incidence of coronary heart disease, essential hypertension and stroke is lower among premenopausal women by comparison with their men counterparts, but it increases in postmenopausal women. In the second year of postmenopause the cardiovascular mortality of women do not differ from the mortality in men. In Hungary – in contrast to United States and Western Europe- the cardiovascular mortality of postmenopausal women is increasing. A number of epidemiologic studies support, that postmenopausal hormone replacement therapy has protective effects against cardio- and cerebrovascular diseases, however some data suggest, that some subgroups of population are more susceptible to the early protrombotic effect of the hormone replacement therapy. Sex hormones (primarily estrogen) exert diverse actions on the central nervous system. The neural and cerebrovascular consequences of conventional menopausal hormone therapy by female sex hormones are also controversial. Because these controversial data, this is a very important question, whether female sex hormones have effects and how on vasculature of the central nervous system and reactivity of cerebral blood vessels.

Aim

The aim of this study was to investigate the effects of ovariectomy and female sex hormone therapy on (1) regional hypothalamic blood flow (2) autoregulation of hypothalamic blood flow (3) $CO_2$-sensitivity of hypothalamic blood flow and hemispheric cerebral blood volume

1. In steady-state conditions:
   1.1. the effect of ovariectomy on regional hypothalamic blood flow
1.2. the effect of estradiol-monotherapy after ovariectomy on regional hypothalamic blood flow
1.3. the effect of medroxy-progesterone-monotherapy after ovariectomy on regional, hypothalamic blood flow

2. During changes of systemic mean arterial pressure:
   2.1. the effect of ovariectomy on the lower limit of autoregulation of hypothalamic blood vessels
   2.2. the effect of estradiol-monotherapy after ovariectomy on the lower limit of autoregulation of hypothalamic blood vessels
   2.3. the effect of medroxy-progesterone-monotherapy after ovariectomy on the lower limit of autoregulation of hypothalamic blood vessels

3. During changes of arterial concentration of CO2 (PaCO2):
   3.1. the effect of ovariectomy on CO2-sensitivity of hypothalamic blood vessels
   3.2. the effect of estradiol-monotherapy after ovariectomy on CO2-sensitivity of hypothalamic blood vessels
   3.3. effect of medroxy-progesterone-monotherapy after ovariectomy on CO2-sensitivity of hypothalamic blood vessels
   3.4. effect of combined (estrogen+medroxy-progesterone) therapy after ovariectomy on CO2-sensitivity of hypothalamic blood vessels
   3.5. the effect of ovariectomy on CO2-sensitivity of hemispheric blood volume
   3.6. the effect of estradiol-monotherapy after ovariectomy on CO2-sensitivity of hemispheric blood volume
   3.7. effect of medroxy-progesterone-monotherapy after ovariectomy on CO2-sensitivity of hemispheric blood volume
   3.8. effect of combined (estrogen+medroxy-progesterone) therapy on CO2-sensitivity of hemispheric blood volume
Methods

Animals

Experiments were carried out in 87 adult, sexually matured, virgin, female Sprague-Dawley rats weighing 200-240 g at the beginning of the study.

Preparation

We divided the animals into two groups:

1. in the control group of rats (n=25) sham-operation (laparotomy) was carried out
2. in another group of animals (n=62) after laparotomy bilateral ovariectomy was performed under intraperitoneal anesthesia (Nembutal 40 mg/kg i.p.; Phylaxia-Sanofi, Budapest, Hungary) during sterile conditions. We divided the ovariectomized animals into four parts:

One quarter of the ovariectomized rats (n=17) received estrogen replacement “OVX+E”: estradiol propionate 450 μg/kg per week, intramuscularly. Another quarter of the ovariectomized rats (n=18) received progestin replacement “OVX+P”: medroxy-progesterone-acetate (MPA) 15 mg/kg once per two weeks, intramuscularly.

The third quarter of the ovariectomized rats (n=8) received combined, estrogen and progestin replacement “OVX+C”: estradiol propionate 450 μg/kg per week and medroxy-progesterone-acetate (MPA) 15 mg/kg once per two weeks intramuscularly.

The last quarter of the ovariectomized animals (n=19) were given only the vehicles (sunflower oil and normal saline) of the sex hormones once per week intramuscularly.

The estradiol propionate (Biogal; Debrecen, Hungary) was freshly prepared in sunflower oil (0.9 mg/ml), the medroxy-progesterone-acetate (Depo-Provera; Upjohn, Puurs, Belgium) was dissolved in normal saline (30 mg/ml). These treatments were applied for 4 weeks after the operation. Upon earlier studies with the same protocol, active hormone treatments resulted in nearly physiologic hormone levels. The animals were anaesthetized with intraperitoneally administered (40 mg/kg) potassium-pentobarbital (Nembutal, Phylaxia-Sanofi, Hungary).

Experimental procedure

After four weeks of treatment, the animals were anaesthetized with Urethane intraperitoneally (1.3 g/kg ethyl-carbamate, SIGMA; St. Louis, MO, USA), artificially ventilated (Harvard, Dual Phase Control Pump, South Natick,
MA, USA), and their body temperature was kept constant at 37 °C with a controlled heating pad. Cannulas were inserted into both femoral arteries (to measure blood pressure and to withdraw blood samples) and into the left femoral vein (for drug administration: urethane for preserving anesthesia and heparin (SIGMA; St. Louis, MO, USA) in a dose of 200U/kg to prevent blood clothing).

**Measurements**

**Measurement of hypothalamic blood flow**

Regional hypothalamic blood flow (HBF) was determined by Aukland’s H2-gas clearance method. Teflon coated platinum (Pt)-electrodes (Medwire, Mt Vernon, NY), 100 µm in diameter, were inserted with stereotaxic instrument into the mediobasal hypothalamus. H2 washout curves (produced by H2-gas inhalation) were recorded on the polygraph together with the systemic mean arterial blood pressure (MAP) (Model 7E, Grass Instruments, Quincy, MA). HBF values were calculated with a computer program, by using the initial slope technique. Data are represented in ml/g/min.

**Measurement of cerebral blood volume**

Measurement of cerebral blood volume: the head of the rat was secured in a stereotaxic head-holder. The CBV was measured by Tomita’s photoelectric method with Sándor’s modification. Through a hole (1.3 mm in diameter) of the skull a miniaturized light source (1 mm wide, 1.5 mm long tungsten lamp (Hamai Electric Co., Tokyo, Japan)) was positioned between the two hemispheres and was fixed with dental cement. Photodiode (SBC-55 Silicon Blue Photodiode, Sharp Electric Co., Tokyo, Japan) was attached at the outside of the skull to the internal lamina of the parietal bone and were secured with light-absorbent dental cement. Assuming that the light intensity, the distance between the lamp and the photodiode, and the light extinction caused by the brain tissue, remain unchanged during the experiment, the light intensity changes are depending on the changing blood content of the transilluminated brain tissue (one of the two hemisphere of the cerebrum), and can be quantified for hemispheric blood volume changes. CBV values were expressed in volume %.

**The autoregulatory test**

Systemic mean arterial pressure was lowered in a stepwise manner from normotensive control values to 80, 60, and 40 mm Hg by a standardized method of blood withdrawal from the femoral artery into a pressurized reservoir system. HBF was determined at each subsequent arterial pressure level. The lower limit of cerebral blood flow autoregulation was determined.
as the highest MAP level at which HBF started to decrease significantly, compared to the steady-state control HBF value.

The CO₂-sensitivity
The hemispheric CBV was recorded continuously, the HBF was measured once in normocapnic (at 36-39 mmHg PaCO₂), hypercapnic (52-57 mmHg PaCO₂) and hypocapnic (26-31 mmHg) conditions. Hypercapnia was produced by 5% CO₂ gas inhalation, the hypocapnia was obtained by increasing the rate of the respiration. The measurements at each PaCO₂ level were performed after a period of at least 10 minutes at the desired PaCO₂ level to ensure that after each PaCO₂ change a new steady-state was attained. There was an approximate period of 25-30 min between each consecutive PaCO₂ level alteration.

Data analysis
All values are presented as mean ± SEM; n represents the number of animals. P<0.05 was considered as a limit of statistical significance. Physiological parameters obtained from the different groups in normocapnic conditions were compared by one-way analysis of variance (ANOVA) and with the Newmann-Keuls or Tukey’s multiple-comparison procedure. To determine the CO₂-sensitivity, statistical comparison were performed between the initial values and those obtained at different CO₂ levels within each of the five different groups (repeated-measures ANOVA). To determine the lower limit of autoregulation, statistical comparisons were performed between the initial HBF values and those obtained at different pressure levels within each of the four different experimental groups (repeated-measures ANOVA).

Results

Effect of ovariectomy, estrogen and progesterone-replacement on steady-state hypothalamic blood flow

Steady-state HBF was significantly decreased in the ovariectomized group of animals (HBF= 0,65±0,08 ml/g/min, n=7) compared to the sham-operated control rats (HBF= 0,92±0,09 ml/g/min, n=10). Estrogen replacement resulted in a complete restoration; HBF values (HBF= 0,89±0,13 ml/g/min, n=7) did not differ statistically from that of the sham-operated controls.
Progestin replacement did not cause such changes; HBF remained significantly lower (HBF= 0,59±0,08 ml/g/min, n=9) compared to the control group (Figure 1).

![Graph showing hypothalamic blood flow (HBF) for different groups: Kontroll, OVX, OVX+Ö, OVX+P. Values are presented as mean ± SEM, p<0.05 was considered as a limit of statistical significance.]

Figure 1.
The hypothalamic blood flow of sham-operated (controll, n=10); ovariectomized (OVX, n=7); ovariectomized+estrogen replaced) (OVX+E, n=7) and ovariectomized+progestin replaced (OVX+P, n=9) animals. All values are presented as mean ± SEM, p<0.05 was considered as a limit of statistical significance. (1) the hypothalamic blood flow is significantly lower in ovariectomized and progestin-replaced animals compared to control animals (2) estrogen replacement caused a complete restoration.

**Effect of ovariectomy, estrogen and progesterone-replacement on HBF autoregulation**

HBF of the sham-operated rats (control group) was well regulated during stepwise hemorrhagic hypotension and remained unchanged when MAP was decreased from 95±3 mm Hg (HBF= 0,92±0,09 ml/g/min, n=10) to 79±1 mmHg (HBF= 0,78±0,05 ml/g/min, n=10) Reduction of the HBF became significant only when the arterial pressure was further decreased to 60±1 mm Hg (HBF= 0,71±0,1ml/g/min, n=10) and to 40±1 mm Hg (HBF= 0,58±0,07 ml/g/min, n=10) respectively. (Figure 2). Ovariectomy (OVX group) resulted in a significant downward shift of the lower limit of HBF autoregulation. In these rats the initial flow (HBF=0,65±0,08 ml/g/min, n=7) did not change at 80 mm Hg
(HBF=0.58±0.07 ml/g/min, n=7) and at 60 mm Hg (HBF=0.55±0.09 ml/g/min, n=7) and was reduced substantially only at the third step of hemorrhagic hypotension, at 40 mm Hg (HBF=0.46±0.07 ml/g/min (n=7) (Figure 2).

Steady-state control HBF (HBF=0.89±0.01 ml/g/min, n=7) of the OVX+E group did not change when systemic MAP was lowered from 98±3 mmHg to 79±1 mmHg (HBF=0.82±0.16 ml/g/min, n=7). Further decrease of the MAP to 60±1 mm Hg (HBF=0.59±0.05 ml/g/min, n=7) and to 40±1 mm Hg (HBF=0.44±0.043 ml/g/min, n=7) caused a statistically significant decrease of the HBF compared to the pre-bleeding control value. (Figure 2).

In the OVX+P animals, hypothalamic blood flow reduction became significant already when the arterial pressure was decreased to 60±1 (HBF=0.41±0.05 ml/g/min, n=9) and to 40±1 (HBF=0.39±0.05 ml/g/min, n=9) compared to the control value (HBF=0.59±0.08 ml/g/min n=9) (Figure 2).

Figure 2.
The hypothalamic blood flow of the four groups of animals (control=sham-operated (n=10); OVX=ovariectomized (n=7); OVX+E= ovariectomized + oestrogen-replaced (n=7); OVX+P= ovariectomized progesterone-replaced (n=9) In steady-state
conditions and at the three steps of haemorrhage (steady-state, at 80 mmHg, at 60 mmHg and at 40 mmHg MAPs respectively). Data are presented by mean±SEM. *= p<0.05 compared to the flow value at the same pressure level in the control animals.

In ovariectomized animals the hypothalamic blood flow decreased significantly only at 40 mmHg MAP value. Estrogen and progestin restored this changes of hypothalamic blood flow autoregulation.

The CO₂-sensitivity of cerebral blood volume (CBV) and hypothalamic blood vessels

Effect of ovariectomy, estrogen-, progesterone- and combined hormone replacement on CBV during hypocapnia and hypercapnia

In the overiectomized animals (OVX group, n=6) the CBV increased statistically during hypercapnic condition (CBV=5,52±0,16 volume%) compared to the normocapnic, steady-state value (CBV=4,84±0,07 volume%). During hypocapnia the CBV did not differ from the normocapnic CBV value (CBV=5,07±0,3 volume%). (Figure 3.)

In the OVX+E group of animals (n=10) the CBV remained unchanged during hypercapnia (CBV=5,37±0,26 volume%) and hypocapnia (CBV=4,87±0,3 volume%) too compared to the steady-state normocapnic value of CBV (CBV=4,85±0,12 volume%). (Figure 3.)

Progesterone replacement (OVX+P n=9) resulted similar changes to be found in the ovariectomized group of animals. The CBV rised significantly during hypercapnia (CBV=5,96±0,15 volume%) compared to the normocapnic, steady-state value of CBV (CBV=4,96±0,15 volume%). The hypocapnic CBV (CBV=4,65±0,4 volume%) did not differ from the normocapnic CBV value. (Figure 3.)

In the combined (estrogen and progestin) replaced group of animals (OVX+C, n=6) the global cerebral blood flow did not change significantly either at hypercapnic (CBV=5,53±0,25 volume%) or at hypocapnic (CBV=4,56±0,47 volume%) condition compared to the steady-state normocapnic CBV values (CBV=4,91±0,13 volume%). (Figure 3.)
CBV of the five experimental groups: control=sham operated (n =10); OVX=ovariectomized (n =6); OVX+E = ovariectomized +estrogen-replaced (n=10); OVX+P=ovariectomized+progestin-treated (n=9); OVX+C= ovariectomized+ estrogen+ progestin replaced (n=6) in steady-state (normo), at hypercapnic (hyper) and at hypocapnic (hypo) conditions. Data are presented as the mean±SEM. * and **p≤0.05: compared to the steady-state CBV value within the same experimental group. The lack of estrogen results a higher CO2-sensitivity of CBV.

Effect of ovariectomy, estrogen-, progesterone- and combined hormone replacement on CO2-sensitivity of hypothalamic blood flow

Hypercapnic sensitivity

In ovariectomized animals (OVX, n=12) the hypercapnic CO2-sensitivity was statistically significant higher compared to the sham-operated .(control, n=15) animals. In ovariectomized+estrogen treated animals (OVX+E, n=9) the CO2-sensitivity was lower, similarly to control animals.
In progesterone- (OVX+P, n=9) and combined (estrogen+progesterone) (OVX+C, n=8) hormone replaced animals the hypercapnic CO₂-sensitivity was statistically significant higher compared to the sham-operated animals. (Table 1.)

**Hypocapnic sensitivity**

The hypocapnic sensitivity of hypothalamic blood vessels did not differ statistically after ovariectomy and hormone replacements compared to the control group of animals. (Table 1.)

<table>
<thead>
<tr>
<th>Group</th>
<th>Hypercapnia</th>
<th>Hypocapnia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0,31±0,23</td>
<td>0,86±0,45</td>
</tr>
<tr>
<td>OVX</td>
<td>*1,42±0,5</td>
<td>0,55±0,85</td>
</tr>
<tr>
<td>OVX+E</td>
<td>0,61±0,67</td>
<td>0,87±0,62</td>
</tr>
<tr>
<td>OVX+P</td>
<td>*1,32±0,26</td>
<td>1,43±0,4</td>
</tr>
<tr>
<td>OVX+C</td>
<td>*0,96±0,12</td>
<td>0,46±0,45</td>
</tr>
</tbody>
</table>

Table 1.

The regional, hypothalamic CO₂-sensitivity during hypocapnia and hypercapnia of the sham-operated (control); ovariectomized (OVX); ovariectomized + oestrogen-replaced (OVX+OE); ovariectomized + progesterone-replaced (OVX+P); and ovariectomized+combined (OVX+C) hormone replaced groups of animals. Data are presented as the mean±SEM. * =p≤0,05: compared to the control group of animals. The CO₂-sensitivity of hypothalamic blood vessels increased after ovariectomy, which change was eliminated after estrogen replacement. There was not difference in hypocapnic sensitivity of hypothalamic blood vessels between the five groups of animals.

**Changes of PaCO₂**
In the five groups of animals the grade of a hypercapnia and hypocapnia did not differ statistically from the normocapnic PaCO$_2$ value. (Table 2.)

<table>
<thead>
<tr>
<th>PaCO$_2$ Hgmm</th>
<th>Group</th>
<th>Normocapnia</th>
<th>Hypercapnia</th>
<th>Hypocapnia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control $\ n=15$</td>
<td></td>
<td>37,44±0,41</td>
<td>*52,65±0,83</td>
<td>*28,63±1,08</td>
</tr>
<tr>
<td>OVX $\ n=12$</td>
<td></td>
<td>37,71±0,71</td>
<td>*53,35±0,86</td>
<td>*29,96±0,74</td>
</tr>
<tr>
<td>OVX+E $\ n=9$</td>
<td></td>
<td>38,32±0,43</td>
<td>*52,35±1,05</td>
<td>*30,63±0,7</td>
</tr>
<tr>
<td>OVX+P $\ n=9$</td>
<td></td>
<td>38,2±0,56</td>
<td>*56,72±1,75</td>
<td>*30,74±0,7</td>
</tr>
<tr>
<td>OVX+C $\ n=8$</td>
<td></td>
<td>37,18±0,24</td>
<td>*53,41±0,87</td>
<td>*26,98±0,88</td>
</tr>
</tbody>
</table>

Table 2. The PaCO$_2$ values of the five groups of animals at normo-, hyper- and hypocapnic conditions. Sham-operated (control); ovariectomized (OVX); ovariectomized + oestrogen-replaced (OVX+OE); ovariectomized + progesterone-replaced (OVX+P); and ovariectomized+combined (OVX+C) hormone replaced groups of animals. Data are presented as the mean±SEM. * and **p≤0,05: compared to the normocapnic value within each groups. There was not any Pa CO2 difference between the five experimental groups.
Discussion

The aim of our study was to investigate the role of female sex steroids on the cerebral vasculature.

The hypothalamic blood flow

The hypothalamus is one important, sex hormone–dependent cerebral region, that participates in the regulation of sexual behaviour; it regulates sex hormone levels and the menstrual cycle in women. The hypothalamus has an important role in modulating the autonomic nervous system activity and it affects the circulation directly through the neurosecretion of Arg-vasopressin. Neurohumoral regulation of the hypophysis, the so-called hypothalamic-pituitary unit, was systematically studied in detail. The physiologic function of this well-studied brain region is dependent on well-maintained cerebral perfusion. Since the hypothalamus is a sex hormone–dependent brain region, and it regulates sex hormone secretion as well, the question arose in the present study as to whether regional hypothalamic blood flow (HBF) and its regulation are affected by different female sex hormone levels.

We concluded that the female sex hormones have effects on cerebral blood vessels during steady-state and reactive conditions too.

The effects of female sex hormones on steady-state hypothalamic blood flow

We demonstrated, that during steady-state conditions, the regulation of hypothalamic blood flow is sex hormone-dependent. After ovariectomy the hypothalamic tissue blood flow decreased significantly. Selective, chronically estrogen-replacement caused a complete restoration. Selective, chronically progesterone-replacement had no effect against the ovariectomy-caused changes of HBF. We concluded that the regulation of hypothalamic blood flow is estrogen-dependent during steady-state conditions.
The effects of female sex hormones on the autoregulation of hypothalamic blood flow

The autoregulation of cerebral arteries is a very important mechanism, which assures the constancy of cerebral blood flow during changes of systemic mean arterial blood pressure. The autoregulation protects the brain from ischemia and brain oedema.

We demonstrated that the regulation of hypothalamic blood flow is sex hormone-dependent. In the absence of female sex steroids the lower limit of autoregulation decreased significantly. Selective, chronically estrogen-replacement caused a complete restoration. Similarly to estrogen, the selective, chronically progesterone-replacement caused a complete restoration of the lower limit of hypothalamic autoregulation.

We concluded that the regulation of hypothalamic blood flow autoregulation is estrogen- and progesterone dependent too.

The effects of female sex hormones on the CO$_2$-sensitivity of the hypothalamic blood vessels

High CO$_2$-sensitivity is one of the major characteristics of the cerebrovascular bed. High CO$_2$-sensitivity, similarly to other major characteristics of cerebral vessels, has been shown to be influenced by a variety of factors. However, no experimental evidence was found in the literature on the involvement of female sex steroids on CBV, either in normocapnic or in hypercapnic conditions.

We demonstrated that the hypercapnic CO$_2$-sensitivity of the hypothalamic blood vessels is sex hormone-dependent. In the absence of female sex steroids the hypercapnic CO$_2$-sensitivity increased. Selective, chronically estrogen-replacement caused a complete restoration. By contrast the selective, chronically progesterone-replacement did not restore the sensitivity. After a combined (estrogen and progesterone) hormone replacement the sensitivity of hypothalamic blood vessels remained higher.

We concluded that the CO$_2$-sensitivity of hypothalamic blood vessels is estrogen-dependent, that means in the presence of estrogen the sensitivity remains lower. This effect of estrogen decreases after combination with progesterone.
We demonstrated contrast with hypercapnic conditions during hypocapnia the CO$_2$-sensitivity of hypothalamic blood vessels is sex hormone-independent.

**The cerebral blood volume**

The value of CBV may provide basic information about the actual condition of the combined arterial, capillary, and venous compartments of the cerebrovascular bed. Clinically, CBV (together with the volume of the brain parenchyma and the cerebrospinal fluid) is one of the three main factors determining the intracranial pressure.

The effects of female sex hormones on the CO$_2$-sensitivity of hemispheric blood volume

We demonstrated that the CO$_2$-sensitivity of hemispheric blood volume during physiologic female sex hormone levels is low. During hypercapnic and hypocapnic conditions the cerebral blood volume remained unchanged. We demonstrated that the CO$_2$-sensitivity of hemispherial cerebral blood volume is sex hormone dependent. In the absence of female sex steroids the hypercapnic CO$_2$-sensitivity increased. Selective, chronically estrogen-replacement caused a complete restoration. By contrast the selective, chronically progesterone-replacement did not restore the sensitivity. After a combined (estrogen and progesterone) hormone replacement the sensitivity of cerebral blood volume remained low, similarly to control animals.

We concluded that the CO$_2$-sensitivity of hypothalamic blood vessels during hypercapnic conditions is estrogen-dependent, that means in the presence of estrogen the sensitivity remains lower. This effect of estrogen did not change after combination with progesterone.

During hypocapnic conditions the CO2-sensitivity of cerebral blood volume is sex hormone independent.
Conclusions

1) The regional, hypothalamic blood flow (HBF) decreased significantly after ovariectomy.
   a) Estradiol monotherapy prevented this change of HBF
   b) Medroxy-progesterone-monotherapy did not result similar changes, the HBF remained significantly lower

2) The lower limit of hypothalamic autoregulation decreased after ovariectomy
   a) Estradiol monotherapy caused a restoration of the lower limit of autoregulation
   b) Medroxy-progesterone-monotherapy caused a restoration of the lower limit of autoregulation too

3) The CO₂-sensitivity of the hypothalamic blood vessels increased significantly after ovariectomy during hypercapnia
   a) Estradiol monotherapy prevented this increasing
   b) Medroxy-progesterone-monotherapy did not prevent this increasing
   c) Combined (estrogen+progesterone) hormone replacement did not prevent this increasing

4) The CO₂-sensitivity of the hypothalamic blood vessels did not change significantly during hypocapnia

5) The hemispheric, global cerebral blood volume (gCBV) increased significantly during hypercapnia.
   a) Estradiol monotherapy prevented this change of CBV
   b) Medroxy-progesterone-monotherapy did not prevent the changes, CBV remained significantly higher
   c) Combined (estrogen+progesterone) hormone replacement prevented the increasing of CBV

6) The hemispheric, global cerebral blood volume (gCBV) did not change significantly during hypocapnia.
Articles related to the topics of the thesis


Other articles


Presentations

Tudományos Diákköri Konferencia 1998: Fájdalomingerek hatása a thalamus véráramlására és az agyi vértérfogatra kontroll és NO-szintáz bénított patkányokon.
Korányi Tudományos Fórum 1998: Fájdalomingerek hatása a thalamus véráramlására és az agyi vértérfogatra kontroll és NO-szintáz bénított patkányokon.
Magyar Élettani Társaság Vándorgyűlése 1998: Fájdalomingerek hatása a thalamus és a hypothalamus véráramlására és az agyi vértérfogatra kontroll és NO-szintáz bénított patkányokon.
Tudományos Diákköri Konferencia 1999: Fájdalomingerek hatása az agy regionális véráramlására és az agyi vértérfogatra kontroll és NO-szintáz bénított patkányokon.
Magyar Élettani Társaság Vándorgyűlése 1999: Fájdalomingerek hatása az agy regionális véráramlására és az agyi vértérfogatra kontroll és NO-szintáz bénított patkányokon.
Tudományos Diákköri Konferencia 2000: Befolyásolja-e a pCO2 változás a hypothalamus véráramlását és az agyi vértérfogatot kontroll, ovariectomizált és hormonpótolt nőstény patkányokban?