

Autonomic Reactions in Patients Undergoing Total Oophorectomy and Their Changes after Human Fetal Tissue Transplant

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The effect of transplantation of human fetal tissues on the type of autonomic reactions in women of reproductive age after oophorectomy was investigated. The maximal effect of the therapy was observed 1.5-2 months after transplantation, but by the sixth month all parameters returned to baseline. Transplantation of human fetal tissues is contraindicated for patients suffering from essential hypertension.

Key Words: *human fetal tissue transplantation; autonomic reactivity; electrical activity of the brain; postoophorectomy syndrome*

The function of the ovaries during the reproductive period affects not only the neurosecretory hypothalamic-pituitary system, but other compartments of the central nervous system as well, including autonomic and psychoemotional disorders clinically similar to menopause.

Bioactive agents affecting the regeneration of cells and tissues have been used in the treatment of diseases of old age, including menopause, since the Fifties [1,2]. Hence, we deemed it interesting to investigate the effect of human fetal tissue transplantation (HFTT) on the type of autonomic reactions in women of reproductive age undergoing total oophorectomy.

MATERIALS AND METHODS

The function of the suprasegmental portions of the autonomic nervous system (ANS) was studied in 46 women aged 36 to 43 years (mean age 39 ± 1.8) treated with HFTT. The electrical activity of the brain

(EEG), autonomic reactivity during the cold test (keeping the hand in 40°C water for 1 min), and autonomic control of activity during intellectual exercise (simple and complex mental arithmetic) were studied.

Arterial pressure was polygraphically recorded by the continuous nonocclusive method, as was the heart rate and respiration rate; the type and duration of the vascular reaction were assessed from optic plethysmography data, and the type of electrical activity of the brain was recorded. For the EEG, extracranial (bi- and monopolar) recording of the bioelectrical activity of the brain was carried out in all cases with standard leads. The EEG was recorded in alert patients at rest and during exposure to functional loads (continuous diffused light, flickering light stimuli at a rate of 3-30 per second, and dosed hyperventilation for 3 min). The EEG was assessed visually and by plotting histograms for 10-sec periods. The psychoemotional status was assessed by psychoanalysis, a modified method of the Minnesota Multiphasic Personality Inventory, and Spilberg's anxiety and personality test in Khanin's modification.

The majority of patients had been ill for 2-3 years, only three for less time (one year) or longer (4-5 ye-

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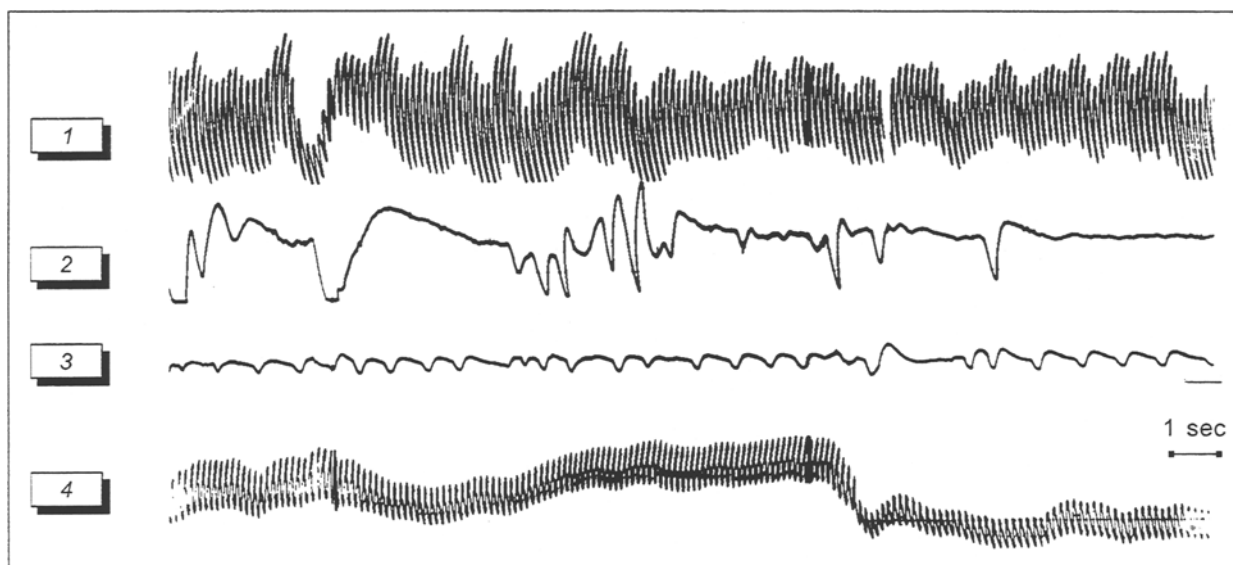


Fig. 1. The sympathoadrenal reaction to cold stimulation. Here and in Figs. 2 and 3: 1) optical plethysmogram; 2) skin galvanic reflex; 3) respiration rate; 4) arterial pressure.

ars). Oophorectomy was carried out for endometrial cysts of the ovaries in 24 patients, and in the rest for pseudomucinous and simple ovarian cysts.

RESULTS

Psychometric testing revealed anxious-depressive neurological disorders in the majority (31) of patients, as well as a high level of personal anxiety on the Spilberg scale (58.5 points with a range of 48 to 76: in age-matched healthy women this score was no higher than 42.6). The anxious-depressive neurological disorders were characterized by internal stress, uncertainty, anxiety, and low spirits. The level of situational anxiety was also elevated.

Patient EEGs showed a reduced L-rhythm (to the point of disappearance), the predominance of more frequent oscillations (β -rhythm), a polyrhythmic α -rhythm, some forms of abnormal activity (groups and bursts of θ -activity), and a liability to reproduce high-frequency rhythms or rhythmic photostimulation, that is, there were signs of boosted work of the activating structures of the brain stem.

Disorders of internal synchronization resulting from functional changes in the activities of various systems of the brain not only disturbed the cerebral homeostasis, but also interfered with the adaptive mechanisms of the whole organism.

The baseline parameters of the autonomic tone in the cardiovascular and respiratory systems showed a tendency toward a drop of the heart rate in the majority of patients (33 out of 46) - 59.6 ± 1.2 (50 to 63) beats/min; 12 patients developed a tendency for tachycardia - 82-84 beats/min, and 10 women presented with normotonia - 70-72 beats/min. In 26 patients ar-

terial pressure was close to normal or below normal (90/60 mm Hg), in 14 it was elevated (135/90 mm Hg), and in just 9 it was normal. The respiration rate was normal in 36 women [15.6 ± 2.1 (15-18) resp/min] and increased in 16 (22-24 resp/min).

The sympathoadrenal reaction to the cold test - an increase of the heart rate by 10-15 beats/min - went along with impairment of the reaction structure during the neuroreflex phase, depending on the excitability of the ANS, while in healthy women the maximal increase of the heart rate (though by no more than 4-5 beats/min) was observed. The heart rate was maximal during the adaptive phase of the reaction, determined by the humoral shifts. A negligible activation of the skin galvanic reflex was observed in one-third of the women, mainly at the beginning of the test (Fig. 1).

Plethysmography showed inertness of the mechanisms of vascular reactivity: vascular hyporeactivity (delayed vascular reaction to the cold stimulus, small amplitude, and protracted course) or areactivity. The wavelike fluctuations of the volumetric pulse were enhanced in patients with elevated arterial pressure (Fig. 2).

Twenty-two women developed a sympathoadrenal reaction to intellectual exercise, which was differently expressed in various systems of the organism.

HFTT brought about the maximal changes in the functional activity of the suprasegmental compartments of the ANS after 1.5 to 2.5 months. The EEG after HFTT showed a tendency toward a recovery of balanced cortico-subcortical interactions. There were fewer pathological bursts of θ -activity. HFTT therapy was associated with signs of increased activity of the sympathetic compartment of the ANS in 30 out of the 46 patients. As early as during the first month of

treatment the majority of patients noted an appreciable improvement of general wellbeing, tone, performance abilities, mood, and sleep; everyday annoyances no longer caused inappropriate, exaggerated negative reactions, and the patients stopped their illness. This was reflected in a reduction of the level of reactive anxiety by 9 to 20 points. In 16 women with a tendency for bradycardia before treatment, the heart rate dropped from 80-82 to 67-65 beats/min; during the first and second month they developed adaptive reactions to functional loads. Marked sympathoadrenal reactions to cold, paradoxical to those before therapy, were recorded: the heart rate increased by 10-15 beats/min, the respiration rate by 4-5 resp/min, and arterial pressure by 10-15 mm Hg. The structure of the reaction was normal in 17 patients, while in 8 a reduction of the reserve potential of the sympathetic compartment of the ANS was observed: the heart rate decreased by 4-5 beats/min even before the cold exposure was over. Fifteen patients exhibited a negative phase of the reaction, as before treatment (Fig. 3).

Before therapy 13 women in this group had complained of up to 10-15 hot flashes a day, marked by a sensation of pressure in the head, heat in the upper body, a suffocating sensation, heavy sweating, chills, and marked weakness; nighttime flashes were particularly unpleasant, as they disturbed sleep and interfered with general wellbeing and sexual activity. When objectively recorded, a hot flash was characterized by a rapid increase of the autonomic parameters to moderate values and their persistence at the maximal level. This corresponded to the type in patients with predominant activity of the vagoinsular (trophotropic)

compartment of the ANS, described for menopausal patients [3]. HFTT brought about a sharp diminution of the number of flashes and reduced their severity, particularly at night. However, during the fifth month after treatment, hot flashes recurred, although they were weaker.

Bradycardia at rest persisted in 13 patients. The cold test showed a 4-5 beats/min increase of the reaction during the neuroreflex phase, whereas during the adaptive phase the level of the reaction was the same. In structure, the reactions approached normal and the negative phase of the reaction disappeared, as did the abnormal respiratory rhythms. In one patient neither the severity nor the number of flashes changed after therapy. In four patients the type of reaction did not change: moderate sympathoadrenal reactions in the cardiovascular system were recorded, with paroxysmal rises of arterial pressure (140/90 and 160/100 mm Hg) and an increase of the respiration rate corresponding to shifts of the heart rate in 2 of these. The negative phase of the reaction persisted in all these patients, although it was less expressed.

Vascular reactions improved in 13 women: the number of vasoconstrictive reactions to the cold stimulus decreased and moderate wavelike fluctuations of the volumetric pulse appeared on plethysmograms with an initially inert curve.

In 4 women neither the baseline values, not the type and degree of reaction changed in the course of therapy. Two of these women suffered from vegetovascular dystonia of the hypertensive type (arterial pressure 150-140/100-90 mm Hg) and had lowered reactions to cold.

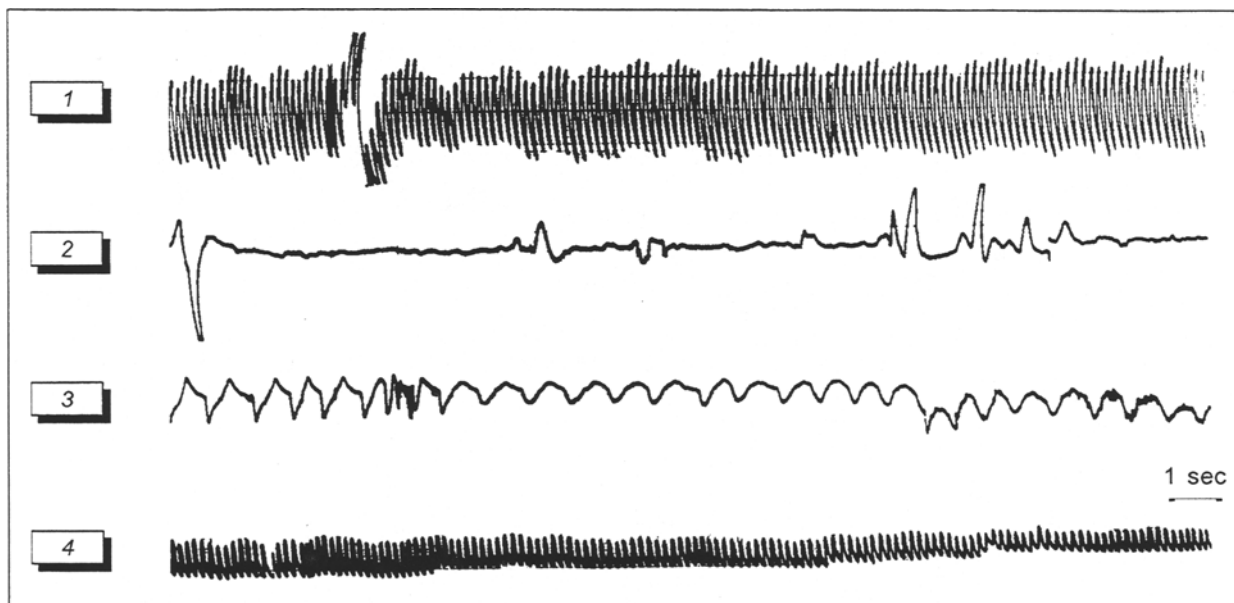


Fig. 2. Absence of sympathoadrenal reaction to cold stimulus (areactivity).

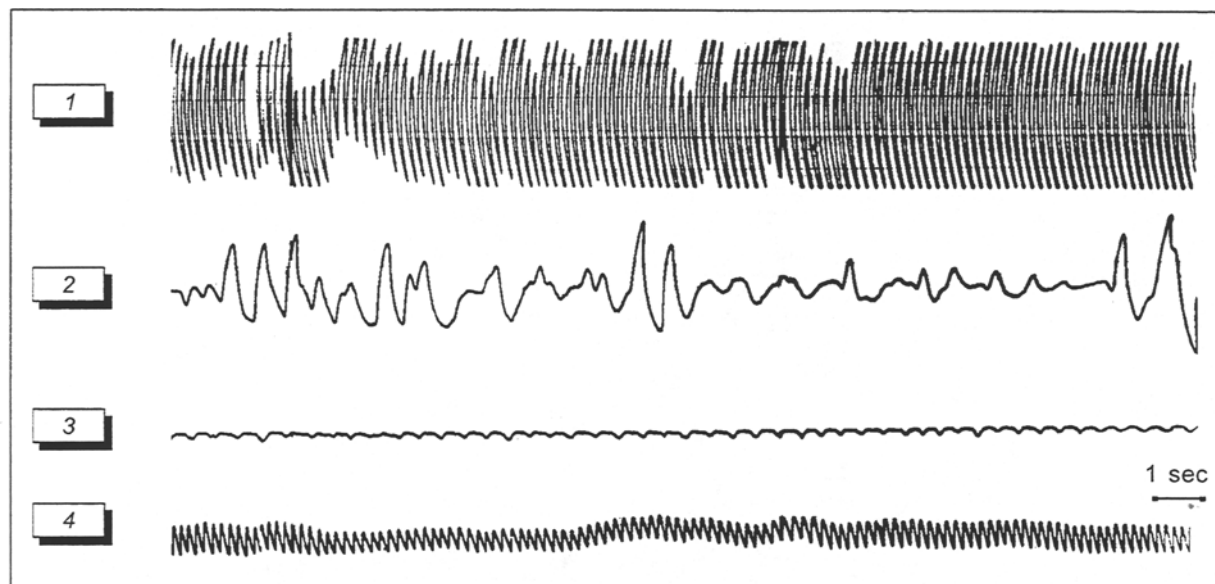


Fig. 3. Reduced (paradoxical) sympathoadrenal reaction to cold stimulus .

In one patient with a hereditary form of essential hypertension HFTT (during the second month) brought about a deterioration of ANS parameters: the heart rate at rest increased by 7-9 beats/min and arterial pressure rose to 200/120 mm Hg; the reaction to cold was perverted: the pulse rate dropped by 4-7 beats/min, the respiration rate by 2-3 resp/min, the level of situational anxiety increased from 41 to 68 points, and vasomotor disorders, such as headache and tinnitus, were aggravated.

More than half of the patients treated with HFTT reacted to intellectual exercise by increased activity of the sympathoadrenal component of the ANS (the increment of the heart rate doubled to become 15-21 beats/min, and the increase of the respiration rate corresponded to the heart rate increase: 4-6 resp/min). Analysis of the type of electrical activity of the brain and autonomic reactions to functional loading showed that the autonomic parameters and patterns of reactions gradually returned to the initial values during the third-fourth month.

Hence, after oophorectomy the pathogenetic profile of all patients of reproductive age consisted of various forms of disintegration of the activities of the nonspecific integrative systems of the brain, primarily

of the limbico-reticular complex, which led to disturbances of adaptive purposeful behavior.

Our data indicate that HFTT has a positive impact on various aspects of the organism's vital activity during the syndrome developing after total oophorectomy. The maximal affect of therapy is observed after 1.5-2 months, but by the sixth month all parameters return to the initial values. For patients with grave psycho-vegetative disorders, particularly in cases of psycho-traumatizing situations, it is desirable to supplement HFTT with psychotherapy and drug correction of the developing disorders. HFTT is apparently not indicated for patients with essential hypertension: for those with vegetovascular dystonia it may be recommended if they complain of asthenia, provided that arterial pressure is monitored over the entire course of treatment.

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