BRAIN BIOCHEMICAL PARAMETERS AND DISTURBANCE OF CONDITIONED REFLEX ACTIVITY OF ORCHIDECTOMIZED RATS

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Aging processes are accompanied by a broad spectrum of interconnected changes in the CNS and hormonal status. Aging is characterized by worsening of memory functions, a catastrophic manifestation of which is senile dementia, accompanied by loss of memory, cognitive activity, and orientation in space [13]. Meanwhile, in the dementias of later life disturbances of glucocorticoid secretion [10, 11] and depression of steroid production, especially sex hormone production [9], are observed. The writers showed previously that orchidectomy in rats, accompanied by a sharp fall of the blood testosterone level, leads to disturbance of the ability of the animals to form a conditioned passive avoidance reflex (CPAR) [3].

The aim of this investigation was to study the central molecular mechanisms involved in memory disturbances caused by orchidectomy.

EXPERIMENTAL METHOD

Behavioral Tests. The investigation was conducted on noninbred male rats weighing 150-180 g. The control and experimental groups each consisted of 30 animals. The rats were kept 10 at a time at a temperature of 21-22°C and a standard 12-hourly light and darkness schedule in standard cages measuring 2145 cm^2. Access to food and water was unrestricted. Orchidectomy was performed under light ether anesthesia and the animals were used in the experiments 30 days after the operation. Animals undergoing a mock operation and intact rats of the same body weight were used as the control. The conditioned-reflex activity of the rats was studied by the standard CPAR method [2]. The rats were placed in the lit compartment of a two-section chamber. After the 1st move from the lit to the dark compartment, unavoidable painful electrical stimulation was applied through the floor in the form of five successive stimuli of alternating current (5 mA), each for a period of 1 sec and with an interval of 2 sec. Animals not visiting the dark compartment in the course of 1 min were withdrawn from the experiment. During testing – the animal was replaced in the lit section after 24 h – the rat remained under observation for 3 min, and the latent period of the move into the dark compartment was estimated. Ability to learn under these conditions was assessed at 80% [2].

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TABLE 1. Effect of Orchidectomy of CPAR Formation and on Some Biochemical Characteristics of the Rat Brain

Group of rats	Latent period of movement of rats from lit into dark compartment, sec	Microviscosity of synaptosomes, conv. units	IUs of synaptosomes, %	Ch of synaptosomes, %	Myelin content in white matter of brain, μg/g wet weight of tissue	AChE activity, %
Intact rats n = 77	164,3±2,2	1,00	47,5±1,5	32,7±1,4	78,13±12,6	100
Rats undergoing mock operation n = 30	163,4±15,6	0,98	46,3±1,7	33,0±1,6	74,1±11,5	99
Gonadectomized rats n = 30	104,4±2,5*	1,28*	33,1±2,2*	42,5±1,0*	49,2±9,0**	69**

Legend: *P < 0.05, **P < 0.01; Chl) cholesterol.

Biochemical Tests. The animals were decapitated immediately after testing of CPAR, the brain was removed, and the cerebral cortex and white matter separated in the cold. Analysis of the lipid composition and calculation of the index of unsaturation of the fatty acids, as well as determination of acetylcholinesterase (AChE) activity were carried out by standard methods [1]. Myelin was isolated from the white matter by the method in [12]. The mass of myelin was determined by drying at 60°C to constant weight. Total protein of myelin was determined by Lowry's method. The results were subjected to statistical analysis by Student's method.

EXPERIMENTAL RESULTS

A statistically significant decrease of 48% in the ability of the gonadectomized rats to form a passive conditioned avoidance reflex was found (Table 1), confirming previous observations [3]. A statistically significant increase of 30% in the cholesterol concentration and a decrease in the index of unsaturation (IUS) of the fatty-acid composition of the synaptosomes by 13% were established in these animals. AChE activity of cerebral cortical homogenates from the gonadectomized rats was 31% lower than that of intact animals. Gonadectomy also was accompanied by a statistically significant decrease in the myelin content in the white matter of the brain by 37.1%; the myelin protein, moreover, was reduced by 2.3 times (12.5 ± 1.5 μg/g myelin) compared with intact rats (29.8 ± 5.5 μg/g).

The investigation thus showed that disturbance of the conditioned-reflex activity of orchidectomized rats is accompanied by several changes in biochemical parameters. Since the trend of these changes coincides with that of disturbances discovered previously in aging rats [2], and also considering that both orchidectomy and aging are accompanied by changes in blood testosterone levels [3, 5], it can be tentatively suggested that there is a certain similarity between the central mechanisms of the memory disturbances during aging and after gonadectomy.

In old age steroid production, especially sex hormone production, is reduced [8]. Since steroid hormones stabilize the content of unsaturated fatty acids [4], it can be postulated that the decrease in IUS of the synaptosomal membranes of orchidectomized and old rats is connected with a decrease in steroid biosynthesis.

An increase in the cholesterol concentration in synaptosomes of orchidectomized rats must be noted. This unique steroid is utilized in the body as a building material in the plasma membranes of the cells and it is also the sole source for synthesis of steroid hormones. According to the physical hypothesis of aging of cells [6] accumulation of cholesterol in the synaptosomes reflects weakening of steroid production, and it evidently also indicates aging of the neurons of orchidectomized rats.

Physiological aging and senile dementia of the Alzheimer type are known to be accompanied by a marked decrease in the myelin content in the white matter of the brain [8, 14]. Moreover, it is claimed that a change (demyelinization) in the white matter, together with senile-atrophic and vaso-atherosclerotic processes, constitute the three fundamental morphologically processes of brain aging, with which the development of dementia in old age is linked [7]. It follows from the facts described above that the reduction in the myelin content which we found on account of the protein component also reflects aging processes in the brain of orchidectomized rats.

It can thus be asserted that disturbances of the brain biochemical parameters which we studied in orchidectomized rats, characterizing the principal systems involved in learning and memory processes, are similar to disturbances taking place during aging. Orchidectomized rats provide a promising model of aging, reflecting interaction between the CNS and endocrine system, which can be used in order to assess the efficacy, and to study the mechanism of action of new potential therapeutic substances for geriatric practice.

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