EFFECT OF AGE, SEX AND GONADAL HORMONE ON BRAIN TISSUE RESPIRATION OF ALBINO RATS*

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Introduction

Metabolic studies in various tissues of animals have been extensively carried out by many workers (Horecker, 1955; Russel, 1951). Physiologically the brain is the controlling and directing centre of the body.

Oxidative glucose metabolism is the primary and indispensable source of energy for brain tissue. It continuously resynthesises energy-rich phosphate compounds in the brain. It is supposed that normal functions are uniquely dependent on an uninterrupted and ample supply of oxygen. It has been shown by many workers that if the cerebral delivery of oxygen is arrested by stopping the cerebral circulation, consciousness is lost in a few seconds. The activities of most of the tissues in the body are altered with age and the change is likely to be related to sex hormones. It was, therefore, decided to make a study of brain tissue metabolism in order to see the influence of age, sex and gonadal hormone on its overall respiration.

Material and Methods

Male and female albino rats of local variety were used throughout the study. The animals were divided into various groups as given in Table I. The rats were decapitated at the time of experiments. QO_2 of the brain was determined by the direct method of Warburg. The oxygen consumption of the brain slices respiring in Krebs Ringer Phosphate Solution (pH 7·2) carrying 2% glucose was measured at 38° C. for 1 hour. Brain slices were cut free-hand with a good safety razor blade. The tissue was excised immediately after the animal was killed and kept at a refrigeration temperature for 2–3 minutes. Slices were then taken, without delay, by chopping. Slices 100 mg. by wet weight were used for the experiment. At the same time 100 mg. by wet weight of tissue slices were kept for the estimation of its dry

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weight. The gas phase was atmospheric air. The reaction was carried out at a shaking rate of 55 oscillations per minute.

TABLE I

Groups of rats used

Group I	..	New-born rats, 10–15 days old.
Group II_M	..	Male rats, weighing between 55 and 95 gm.
Group III_M	..	Male rats, weighing between 120 and 150 gm.
Group IV_M	..	Male rats, weighing over 200 gm.
Group II_F	..	Female rats, weighing between 55–95 gm.
Group III_F	..	Female rats, weighing between 120 and 150 gm.
Group IV_F	..	Female rats, weighing over 200 gm.
Group V_F	..	Female rats, kept as a control over group VI_F.
Group VI_F	..	Female rats, ovariectomised one month previously (initial weight between 50 and 60 gm.)
Group VII_F	..	Female rats, ovariectomised as in Group VI_F and treated with subcutaneous estradiol benzoate 0·5 mg. per day for terminal seven days.

RESULTS AND DISCUSSION

The results are summarised in Tables II, III and IV. It will be seen that there is a rise in oxygen uptake as the weight of the rat increases except in the new born animal where the oxygen uptake is related to dry weight only. However, if the oxygen uptake is calculated on the basis of wet weight then it is found to be lower than in the animals of the next higher age (body weight) group. This difference is probably due to a markedly higher water content of the brain tissue of the new born as compared to that of older animals. In the present study it was observed that whereas in the new born tissue water constituted as much as about 90% of the total wet weight and that in the older group was about 80% only. The value reaches to the maximum when the body weight reaches 150 gm. Then there is a definite fall in the oxygen consumption of the tissue.

Different levels of metabolism can be distinguished in the animals during post-natal life. The metabolism during first 15–20 days of life is characterised by a low oxygen and glucose utilisation. At the age of 10–12 weeks (*i.e.*, when body wight is about 150 gm.) the respiration is highest. The adult level is obtained after about 22–24 weeks (*i.e.*, when body weight of rat is over 200 gm.).

TABLE II

Brain tissue respiration in different groups of male and female rats

Group No.	No. of animals	Body wt. gm. $\pm\sigma$m.*	Mean QO_2: μl. of O_2 uptake/100 mg. wet wt./hr. $\pm\sigma$m.*	Mean QO_2: μl. O_2 uptake/mg. dry wt./hr. $\pm\sigma$m.*
I	6	16·05±1·13	57·27±1·85	4·37±0·17
II_M	6	74·9±4·57	58·44±1·98	2·79±0·02
III_M	6	137·3±4·67	98·28±3·48	4·74±0·156
IV_M	6	217 ±4·67	46·28±2·63	2·29±0·112
II_F	6	72 ±3·01	45·70±2·47	2·3 ±0·154
III_F	6	130 ±3·62	64·8±3·15	2·82±0·056
IV_F	6	225 ±8·11	38·89±1·16	1·80±0·0113

* σm. = Standard deviation of the mean.

Respiratory metabolism of rat brain tissue by slice technique has been studied by many authors (Elliott, 1955; Greengard and McIlwain, 1955). The variation in the values obtained in the present study may be due to the differences in the details of the technique used. Thus we used lower speed of oscillation in the Warburg apparatus (55 oscillations/minute) and used atmospheric air as the gas phase. The variations are certainly too high to be due to difference of strain of the animals.

Koch and Koch (1913) studied the respiratory metabolism of different ages of animals. They conclude that rise in rat brain metabolism coincided with the beginning of myelinisation. They also state that the process continues with great intensity until about 4–7 weeks of life. It is also assumed that the energy required for myelinisation and many other changes occuring during the first month of life result in the high metabolisms found during

this period. Himwich and Fazekas (1941) studied the respiration of different parts of dog brain in relation to age of the animal. They reported that the high values for respiration were related to the particular part of the tissue which has started functioning. Tayler and Harreveld (1942) also obtained curves of the oxygen consumption of various parts of the developing rat brain which resembled curves reported for dog by Himwich and Fazekas.

TABLE III

Brain tissue respiration values in three groups of female rats

Group No.	No. of animals	Body weight gm. ±σm.*	Wt. of brain mg. ±σm.*	Wt. of brain per 100 gm. body weight mg.	Mean QO_2: µl. of O_2 uptake/mg. dry wt./hr./ ±σm.*
V_F (Control)	6	98·6±0·070	1615±16·76	1646·3	2·62±0·013
VI_F (Castrated)	6	125·2±6·71	1471±20·41	1183·2	3·74±0·022
VII_F (Castrated and treated)	6	105·7±6·62	1267±21·76	1208·8	3·13±0·007

* σm. = Standard deviation of the mean.

The studies of the biochemistry of the brain during early life are limited and very few references are available concerning the relationship between biochemical and functional changes. According to some these events are related to the results of the process of myelinisation (Sp rry and Welsch, 1960). Myelinisation, from a physical point of view, is the most conspicuous change in the developing brain.

It seems likely, therefore, that the change in the values of respiration is the reflection of the fuctional activity of the brain.

Donaldson and Hatai (1931) explain that the low oxygen uptake of the infant brain involves the respiratory enzymes concerned in these processes. In the adult brain there is a greater proportion of grey (protein) and white (lipoid) matter. The greater rate of adult brain, therefore, may be correlated with the larger protein contents of the cells.

While studying the effect of sex on brain tissue respiration, it is observed that the values obtained for male rats are higher than those for the females.

TABLE IV

Oxygen uptake of rat brain tissue

GROUP No. I (New Born)

Expt. No.	Body weight in gm.	Dry weight in mg.	Flask No.	Actual uptake in mm.	QO_2 (wet wt.) basis	QO_2 (dry wt.) basis
1	13·0	14·0	24	—70	65·01	4·6
2	12·0	16·0	24	—61	56·65	3·54
3	18·5	13·3	24	—64	59·44	4·57
4	18·5	11·0	24	—55	51·08	4·64
5	17·3	12·0	24	—55	51·08	4·24
6	17·0	13·0	24	—65	60·37	4·64

The study of brain tissue respiration dealing with the factor of gonadal hormone shows that the brain of the castrated female rat has an oxygen uptake 35% higher than of normal rat kept as a control. The brain of castrated female rat treated with estradiol respires at a rate slightly higher than the normal which shows that it has a tendency towards normal value. It may therefore be suggested that female gonadal hormone has an inhibitory action on oxygen uptake. A possible interpretation is that the inhibiting effect of estrogen is decreased after castration and can be prevented for the most part by the administration of estradiol. This also may explain for the higher values in case of male rats than the females of equal weights.

SUMMARY

Effects of age, sex and female gonadal hormone on brain respiration in rats are studied. Oxygen consumption of the entire brain of rat rises as the weight of animal increases. It is maximum when the body weight reaches about 150 gm. Then there is a decrease in oxygen consumption. Female sex hormone seems to have an inhibitory action on the brain respiration.

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