On the Intermediate Metabolism of Carbohydrates in the Brain of Hypertensive and Postapoplectic Patients

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On 25 cases of hypertension and 16 cases of postapoplectic patients the cerebral carbohydrate metabolism was estimated, simultaneously with the cerebral hemodynamics, using Kety's \( N_2O \) method. The cerebral glucose consumption was generally smaller in these patients than that of healthy subjects. It was found not to stand in such a close relationship with cerebral oxygen consumption as it was the case in healthy subjects. It depends on the glucose content in arterial blood to some extent. Some disturbances are presumed in the blood glucose transfer into the brain tissue. No significant difference was detected between the hypertensive and the postapoplectic subjects in respect of the cerebral glucose consumption. An increased lactic acid formation was presumed in the brain of these patients, especially in the hypertensive patients: The amount of lactic acid carried out of the brain was in many cases too large to be explained by the decrease in oxidized part of blood glucose owing to the reduced oxygen supply.

Since the \( N_2O \) method devised by Kety has been introduced into the clinical investigations, the cerebral hemodynamics were elucidated in the area of hypertensive diseases and of postapoplectic states. To date, the present authors\(^1\) have investigated the cerebral hemodynamics in postapoplectic state, in which a derangement of blood flow and a decrease of oxygen consumption in the brain were confirmed. A similar tendency was demonstrated also in many instances of hypertension by Tateyama\(^2\) and others, even though it was in a comparatively slighter degree.

The authors further investigated the cerebral carbohydrate metabolism in these
patients. As to the intermediate metabolism of carbohydrate in the brain of aged healthy subjects, it has been pointed out in our another report that the metabolism was lowered in a well balanced equilibrium, presumably owing mainly to the senile hypofunction of the brain tissues. In the present paper the authors report on the carbohydrate metabolism in the brain of hypertensive and postapoplectic patients. There are many difficulties in the evaluation of the results, because the metabolized amount had to be calculated from the small differences in carbohydrate contents in the blood specimens.

EXPERIMENTALS

METHOD

On 25 cases of hypertensive patients the mean blood pressures of which are ranging from 130 to 104 mm of mercury and 16 cases of postapoplectic patients with moderate hypertension (with mean blood pressure ranging from 125 to 105 mm of mercury), in various age ranges, the carbohydrate metabolism and the hemodynamics in the brain were simultaneously measured by the same method as employed in the former report.

RESULTS

1. **Cerebral glucose consumption**

In general, the cerebral glucose consumption in hypertensive and postapoplectic patients was found markedly lower than that of healthy subjects. The difference was statistically significant ($P<0.05$). The close relation between the decrease of cerebral glucose and the rise of age, as found in healthy group, could

![Fig. 1. Cerebral glucose consumption and aging.](image-url)
not be detected in these patients (Fig. 1). Also the parallelism between the cerebral glucose consumption (CMRgl) and the cerebral oxygen consumption (CMRO₂), which was found in healthy subjects, was not apparent (Fig. 2). In these patients, any relationship between A-Vg1 and CBF could not be detected (Fig. 3).

On the other hand, a significant parallelism between the arterial glucose content (Agl) and A-Vg1 was observed, a finding which could not be demonstrated in healthy subjects. The glucose consumption was lower in these patients than in healthy persons, but not owing to the lowered arterial glucose content, because
no difference in Agl could be detected between these patients and healthy subjects. The decreased glucose consumption was rather dependent upon the decrease cerebral glucose consumption rate, as shown in Fig. 4.

Fig. 4. Cerebral arterial glucose contents and arteriovenous glucose differences.

The ratio of CMRO₂ to CMRgl is generally increased in hypertensive and postapoplectic patients. Numerically, the difference between hypertensive patients and healthy persons is significant, while that between postapoplectic and healthy subjects, and that between hypertensive and postapoplectic patients we not significant (Fig. 5).

Fig. 5. Glucose oxidation rate in the brain.
2. *Intermediate metabolism of pyruvic acid*

In both groups of patients, the difference between pyruvic acid in venous blood and that in arterial blood (V-A pyr) was to some extent greater than that in healthy persons. No close relation could be detected between the cerebral pyruvic acid outflow and CMRO$_2$ or aging in those patients. (Fig. 6)

3. *Intermediate metabolism of lactic acid*

In both diseases, also, the difference between the lactic acid content in venous blood and that in arterial blood (A-V lac) in general was greater than that of healthy persons. The values of cerebral lactic acid outflow were larger in those patients than in healthy subjects, extremely larger in some cases of hypertension, but the difference was not statistically significant. No correlation could be found between the cerebral lactic acid outflow and CMRO$_2$ or aging in those patients (Fig. 7).

4. *The ratio of outflow of cerebral lactic acid to that of cerebral pyruvic acid (V lac/V pyr)*

The ratio of the amount of lactic acid carried out of the brain to that of pyruvic acid is much greater in these diseases than in healthy subjects. A significant difference (P<0.05) is shown between hypertensive and healthy groups, the ratio being smaller in the postaploptics than in the hypertensives. This finding means a certain change occurring in the oxidative process of carbohydrate metabolism in the brain in those patients (Fig. 8).

5. *Mutual relationships among CMRg1, rate of cerebral oxidation of glucose, and outflow of cerebral pyruvic and lactic acids*

In healthy subjects, the sum of the amounts of oxidized glucose calculated from CMRO$_2$, lactic and pyruvic acid outflows was nearly coincident with the cerebral glucose consumption. But in these diseases the cerebral glucose con-
Fig. 7. Lactic acid carried out of the brain and cerebral oxygen consumption.

Fig. 8. The ratio of lactic acid to pyruvic acid carried out of the brain.

sumption is decreased and the lactic acid exportation is markedly increased. Consequently, the sum of amounts of oxidized glucose and lactic and pyruvic and outflows is greater than the cerebral glucose consumption. This finding means that there is a marked unbalance between incoming and outgoing of the cerebral carbohydrates. Of course, there are some exceptional cases in these groups, which
show only little discrepancies in the metabolic balance. As a general tendency, however, a negative metabolic equilibrium in the brain could be recognized. This tendency was more significant in the group of hypertension than that in postapoplectic patents (Fig. 9).

**DISCUSSION**

The carbohydrate metabolism in hypertensive diseases had not yet been fully clarified though its derangement was presumed by some investigators, except for so-called symptomatic hypertension, the pathogenesis of which has been thoroughly investigated.
Our results restricted in the field of cerebral metabolism are also setting many problems obviously. The derangement in the glucose uptake in the brain of the hypertensive as well as the hypertensive postapoptectic patients, as investigated in detail in the present report, are indicating an evident metabolic disorder, the cause of which is presumably much complicated, the effect of high variable blood pressure, the vascular changes in the brain, the drug administered and the altered cellular activity estimated from oxidation rate of glucose in the brain and others have been elaborated, but any simple causalities of these factors could not been confirmed.

As to the lactic acid and pyruvic acid metabolism, the amount of those acids carried out of the brain was exaggerated in both groups of the diseases, while the increased ratio of V-A lac to V-A pyr was smaller in the postapoplectics than in the hypertensives. The cause of these changes may be inferred as follows: In the hypertensive subjects including the postapoplectics, the oxygen supply to the brain is insufficient in general from the view point of tissue demand, resulting in the decreased oxidation of glucose, and consequently the accumulation of lactic acid as well as the increase of transportation of acids from brain tissue into venous blood. The difference between the postapoplectics and the hypertensives may depend upon the severity of cellular damage of brain tissue in each group; the advanced cellular damage in the former would require less oxygen because of their diminished demand of energy, thus the difference between the oxygen demand and supply, represented by the lactic acid production or the ratio of V-A lac to V-A pyr would be smaller than the latter.

However, these explanations are implying an inevitable imperfection. In many instances of both groups the amount of lactic acid carried out of the brain is exceeding the unoxidized part of the consumed glucose. Anaerobic glycolysis of some substances in the brain, the accelerated glycolysis under the existence of something like epinephrine or the other unknown mechanism should be taken into account.

References

2) Tateyama, M., ibid., 1959, 70, 125.