# CARBOHYDRATE METABOLISM OF BRAIN DURING INDUCED MUSCULAR ATROPHY AND WORK OVERLOAD IN THE DOG, *CANIS DOMESTICUS*

Y. DHANANJAYA REDDY, K. VENKATARAMI REDDY, O. RAMAKRISHNA*
S. GOVINDAPPA and P. REDDANNA
*Department of Zoology, Sri Venkateswara University, Tirupati 517502, India.*
** Department of Surgery & Radiology, College of Veterinary Science, Tirupati 517502, India.*

## ABSTRACT

Muscular work overload and atrophy were induced through electrical stimulation and sciatectomy respectively and the impact of the same on brain carbohydrate metabolism was studied in the dog, *Canis domesticus*. Induced muscular training resulted in increased utilization of glycogen and glucose through enhanced glycogenolysis and glycolysis. The citric acid cycle was inhibited along with the lowered mobilization of hexoses into hexose monophosphate pathway. The muscular atrophy, on the otherhand, decreased the utilization of glycogen and glucose through inhibited glycogenolysis, glycolysis, citric acid cycle and HMP shunt. Probable decrease in the efficiency of brain during muscular disuse was suggested.

## INTRODUCTION

ELECTRICAL stimulations have been widely employed to induce localized muscular exercise[1,2]. Electrical stimulation and exercise of 'whole animal' modulated the structure and function of the body involving changes in the metabolic pathways of different tissues[3,4]. The muscular training programme induced through prolonged electrical stimulation could change the carbohydrate metabolism of brain tissue in amphibians[5]. Thus investigations in the metabolism of other tissues during induced muscular overwork might reveal the metabolic interrelationship between muscle and other tissues in the body[6–9]. The present study is aimed at exploring the impact of muscle disuse through denervation and muscle overwork through electrical stimulation on brain carbohydrate metabolism in dog, *Canis domesticus*.

## MATERIALS AND METHODS

For the present study twelve healthy mongreal dogs, *C. domesticus* aged 3–4 years and weighing 11–16 kg were randomly divided into three groups as follows.

Group I: Normal sham-operated dogs designated as "controls" (C)

Group II: Experimental animals with gastrocnemius muscle and one leg electrically stimulated for 15 days called as "stimulated" animals (S).

Group III: Experimental animals with unilateral sciatic denervation termed as "denervated" animals (D).

The sciatic denervation and electrical stimulation were conducted as described earlier[6–9].

Gylcogen[10], glucose[11], lactic acid[12], pyruvic acid[13] and the activity levels of phosphorylase *a* and *b*[14], aldolase[15], succinate$^-$, malate$^-$, lactate$^-$ and glutamate dehydrogenase[16] and glucose-6-phosphate dehydrogenase[17], were estimated in the brain of normal (control) and two experimental categories of dogs. All the enzyme assays were made under the conditions following zero-order kinetics after preliminary standardization regarding linearity with respect to time of incubation and enzyme concentration.

## RESULTS AND DISCUSSION

The results presented in tables 1 and 2 reveal the extent of changes in the brain carbohydrate metabolism of the dog, *Canis domesticus* during muscular work overload and disuse induced through electrical stimulation and sciatectomy respectively. The induced muscular work overload decreased the brain glycogen content significantly, indicating their probable mobilization towards energy release. The elevated activity level of phosphorylase *a* suggests the enhanced glycogenolysis in the brain in response to the induced muscular training. This elevated glycogenolysis might be responsible for the decrease in glycogen content.

**Table 1** *Levels of gylcogen, glucose, pyruvate, lactate (mg/g wet wt) and activity levels of phosphorylase a, ab and b (μmol of pi/formed/mg protein/hr) and aldolase (μmol of FDP-cleaved/mg protein/hr) in the brain tissue of control, stimulated and denervated animals.*

| Component | Control (C) | Stimulated (S) | Denervated (D) | Percent change C *vs* S | Percent change C *vs* D |
|---|---|---|---|---|---|
| Glycogen | 0.521 ± 0.03 | 0.311 ± 0.02 | 0.750 ± 0.06 | −40.30* | +49.95* |
| Glucose | 2.64 ± 0.09 | 2.24 ± 0.07 | 3.19 ± 0.14 | −53.03* | +20.83* |
| Pyruvate | 1.47 ± 0.09 | 2.67 ± 0.12 | 1.02 ± 0.08 | +81.63* | −30.61* |
| Lactate | 3.81 ± 0.12 | 4.64 ± 0.23 | 2.08 ± 0.10 | +21.78* | −45.40* |
| Phosphorylase *a* | 1.54 ± 0.08 | 2.32 ± 0.09 | 0.860 ± 0.05 | +51.23* | −43.93* |
| Phosphorylase *ab* | 2.02 ± 0.13 | 2.82 ± 0.15 | 1.33 ± 0.07 | +39.60* | −34.15* |
| Phosphorylase *b* | 0.486 ± 0.03 | 0.502 ± 0.03 | 0.470 ± 0.03 | +3.29 NS | −3.29 NS |
| Aldolase | 1.02 ± 0.07 | 1.52 ± 0.09 | 0.57 ± 0.03 | +49.21* | −44.12* |

Values are mean of six observations. Mean ± S.D.; + and − indicate percent increase and decrease over control. *p* denotes level of significance and NS, nonsignificance. * $P < 0.001$.

**Table 2** *Activity levels of succinate⁻, malate⁻, lactate⁻, glutamate⁻ and glucose-6-phosphate dehydrogenases (μmol of formazan formed/mg protein/hr) in the brain tissue of control, stimulated and denervated animals.*

| Component | Controls (C) | Stimulated (S) | Denervated (D) | Percent change C *vs* S | Percent change C *vs* D |
|---|---|---|---|---|---|
| Succinate dehydrogenase | 1.02 ± 0.08 | 0.748 ± 0.04 | 0.679 ± 0.04 | −26.66* | −33.43* |
| Malate dehydrogenase | 0.189 ± 0.01 | 0.074 ± 0.005 | 0.112 ± 0.01 | −60.85* | −30.35* |
| Lactate dehydrogenase | 0.30 ± 0.02 | 0.192 ± 0.01 | 0.223 ± 0.02 | −36.00* | −25.66* |
| Glutamate dehydrogenase | 0.228 ± 0.01 | 0.151 ± 0.01 | 0.148 ± 0.01 | −33.77* | −35.08* |
| Glucose-6-phosphate dehydrogenase | 1.32 ± 0.11 | 0.822 ± 0.05 | 0.957 ± 0.05 | −37.63* | −27.38* |

Values are mean of six observations. Mean ± S.D.; + and − indicate percent increase and decrease over control. *P* denotes level of significance. * $P < 0.001$

The overall elevation in the total phosphorylase activity indicates the active *de nono* synthesis of the enzyme itself in the brain tissue. Inspite of elevated glycogenolysis, the tissue glycose content was also decreased suggesting the subsequent utilization of glucose. The observed elevation in the activity level of FDP-aldolase reveals the mobilization of glucose through the hexose diphosphate pathway. As a result of elevated glycogenolysis and glycolysis, probably the pyruvate and lactate might have been accumulated. The activity levels of LDH and GDH were decreased significantly leading to lowered mobilization of lactate and amino acids into citric acid cycle which might be responsible for the inhibition in the activity levels of SDH and MDH and thereby on TCA cycle. This observation in dogs is in consonance with the lowered SDH activity observed in the brain of frog during muscular training[5]. Glucose-6-phosphate dehydrogenase activity level was significantly lowered suggesting the probability of decreased mobilization of glucose into hexose monophosphate pathway. Thus muscular training seems to result in the enhanced utilization of glucose and glycogen through glycogenolysis and glycolysis with lowered oxidative metabolism in the brain tissue.

In contrast, the muscular disuse induced through sciatectomy, resulted in the significant increase in both glycogen and glucose contents in the brain tissue (table 1). The activity levels of phosphorylase *a* was inhibited significantly suggesting the suppression of glycogeno-

lysis. Since the total phosphorylase activity was lowered, an overall decrease in the concentration of enzyme itself can be suggested. FDP-aldolase activity level was also lowered significantly indicating the decreased level of operation of glycolysis which might be responsible for accumulated glucose content observed in the present study. The decrease in the lactate and pyruvate contents also represents lowered glycolysis. The activity levels of NAD-LDH and NAD-GDH were decreased significantly suggesting the decreased mobilization of lactate and amino acids into the citric acid cycle. As a result, the succinate and malate dehydrogenase activity levels were also probably inhibited and thus the oxidative metabolism of brain was inhibited during muscular disuse. The acitivity level of G-6-PDH of the brain tissue was also inhibited revealing the decreased mobilization of glucose into hexose monophosphate pathway. Thus muscular atrophy induced through disuse seems to result in the overall decreased utilization of carbohydrate fuels which might result in the decreased efficiency of brain tissue.

In general, the muscular training seems to enhance the utilization of carbohydrates, whereas the muscular disuse resulted in the decreased utilization of carbohydrates in the brain. Hence the carbohydrate utilization of the brain tissue is in perfect correlation with the extent of muscular work in the body.

## ACKNOWLEDGEMENTS

The authors YDR and KVR are thankful to ICMR and CSIR, New Delhi for financial assistance.

4 September 1984; Revised 30 March 1985

1. Herbison, G. J., Teng, C. and Bordan, E. E., *Arch. Physiol. Med.*, 1973, **54**, 156.
2. Pette, D., Smith, M. E., Slatudte, H. W. and Verbova, G., *Pfluger. Arch.*, 1973, **338**, 257.
3. Poortmans, J. R., Labilloy, D. and Hoceyoux, J., *Rey. Mediter. Sci. Med.*, 1978, **2**, 35.
4. Sparks, H. V., *Fed. Proc. Am. Exp. Biol.*, 1980, **39**, 1547.
5. Reddanna, P. and Govindappa, S., *Curr. Sci.*, 1978, **47**, 756.
6. Venkata Rami Reddy, K., Dhananjaya Reddy, Y., Govindappa, S. and Reddanna, P., *Arch. Int. Physiol. Bioch.*, 1983, **91**, 411.
7. Venkata Rami Reddy, K., Dhananjaya Reddy, Y., David, E., Rama Krishna, O., Govindappa, S. and Reddanna, P., , *Proc. Indian Natl. Sci. Acad.*, 1984a, **B50**, 37.
8. Venkata Rami Reddi, K., Dhananjaya Reddy, Y., Ramakrishna, O., Govindappa, S. and Reddanna, P., *Proc. Indian Natl. Sci. Acad.*, 1984b, **50**, 249.
9. Venkata Rami Reddy, K., Ramakrishna, O., Govindappa, S. and Reddanna, P., *Proc. Indian Natl. Sci. Acad.*, 1984c, **B50**, 304.
10. Kemp, A. and Van Heijningen, M. K., *Biochem. J.*, 1954, **56**, 646.
11. Mendal, B., Kemp, A. and Myers, D. K., *Biochem. J.*, 1954, **56**, 639.
12. Barker, S. B. and Summerson, W. H., *J. Biol. Chem.*, 1941, **138**, 000.
13. Friedmann, T. E. and Haugen, G. E., *J. Biol. Chem.*, 1942, **147**, 67.
14. Cori, G. T., Illingworth, B. and Killer, P. G., *Methods Enzymol.*, 1955, **1**, 200.
15. Bruns, F. H. and Bergmeyer, H. U., *Methods in enzymatic analysis*, (ed.) H. U. Bergmeyer, Academic Press, New York, 1965, 724.
16. Reddanna, P. and Govindappa, S., *Curr. Sci.*, 1978, **47**, 531.
17. Bergmeyer, H. U. and Bruns, F. H., *Methods in enzymatic analysis*, (ed.) H. U. Bergmeyer, Academic Press,,s,s, New York.
18. Von Glutz, G., Luthi, U. and Howald, H., *Proc. Phys. Perform. Muscle Metabol.*, (eds) O. Hannimen and Harris, Kupio Publishers, Finland, 1976.