Maximum Oxygen Consumption and Catecholamines in Thyroidectomized Dogs

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Abstract. Comparisons have been made in 7 dogs between maximum oxygen consumption recorded before (N dogs) and after thyroidectomy (T dogs). The comparisons were performed under two conditions 1) during severe cold stress ($C_{VO_2 \text{max}}$), 2) during a short period of exhaustive work ($Ex \, V_{O_2 \text{max}}$). Heart rate, plasma catecholamine and substrate concentrations (glucose, lactic acid, FFA) were measured under each condition.

1. Thyroidectomy induced a more substantial decrease in $C_{VO_2 \text{max}}$ than in $Ex \, V_{O_2 \text{max}}$.

2. At $C_{VO_2 \text{max}}$, average plasma epinephrine and norepinephrine concentrations rose to a higher level in T dogs than in N dogs. In T dogs, correlations were found between plasma epinephrine concentrations and $C_{VO_2 \text{max}}$ values, and between plasma norepinephrine concentrations and $C_{VO_2 \text{max}}$ values. At $Ex \, V_{O_2 \text{max}}$, average plasma norepinephrine concentrations were similar in N dogs and in T dogs, and average plasma epinephrine concentrations were not significantly different from each other.

3. At $Ex \, V_{O_2 \text{max}}$, average plasma concentrations of the various substrates were not significantly different in N dogs and T dogs. At $C_{VO_2 \text{max}}$, plasma FFA levels were higher in T dogs.

It may be concluded that in dogs, thyroidectomy affects mechanisms which are more specifically involved in heat production than in muscular exercise. The increased catecholamine secretion in response to cold which occurred in T dogs appeared merely to limit the decrease in heat production. It seems possible that increased catecholamine secretion compensates for the decreased sensitivity of β receptors to catecholamine but it cannot fully account for the effects of thyroidectomy.

Key words: Maximal oxygen consumption — Cold — Exercise — Thyroidectomy — Plasma — Catecholamine — Glucose — FFA — Lactic acid

Introduction

It is accepted that the greatest increase in metabolic rate are induced by muscular exercise and cold exposure. It may be assumed that under both conditions skeletal muscle is the effector as shivering is the main source of thermogenesis in dogs exposed to an acute cold stress (Chatonnet 1961). An increase in metabolic rate involves both cardiovascular adjustments and an increase in the mobilization and utilization of energy substrates and catecholamines are known to play an important role in these changes (Himms-Hagen 1967). Moreover during exercise the increase in plasma catecholamine concentration was found to be related to the intensity of exercise (Haggendal et al. 1970; Galbo et al. 1975), and during cold exposure the increase in plasma catecholamine concentration was related to the fall in core temperature (Johnson et al. 1977; Therminarias et al. 1979). A further study performed in dogs during short exhaustive work ($Ex \, V_{O_2 \text{max}}$) and during a severe cold stress ($C_{VO_2 \text{max}}$) showed that plasma catecholamine concentrations reached similar very high levels in the two conditions (Lucas et al. 1980).

It is also well established that thyroid hormones influence the metabolic rate and play an important role in the maintenance of body temperature: these effects may be achieved by a direct action or by interaction with catecholamines for thyroid hormones are known to sensitize animals to the cardio vascular, glycogenolytic and lipolytic effects of catecholamines (Rosenberg and Bastomsky 1965). Theoretically therefore thyroidectomy might be expected to reduce maximum oxygen consumption. Indeed a moderate decrease in maximum oxygen consumption during an exposure to an acute cold stress has already been observed after thyroidectomy in rats (Freely et al. 1961), and in spinal dogs (Tanche and Therminarias 1969). Although the more rapid fall of body temperature observed in hypothyroid rat has been related to a more rapid loss of body heat rather than to a reduce rate of heat production (Freely et al. 1961). During exercise, only a few studies have been performed at maximum work load: Baldwin et al. 1980, have recently reported that a moderate decrease in maximum oxygen consumption occurred in hypothyroid rats, but it has also been shown that hypothyroid men are able to perform heavy exercises (Barack et al. 1971).

Since in the hypothyroid state an increase in urinary excretion of catecholamines has been observed at neutral temperature and during cold exposure (Andersson et al. 1967; Canguilhem and Malan 1971; Gale et al. 1971), it has been proposed that an enhanced secretion of catecholamines by the sympathtico-adreno-medullary system may enable hypothyroid animals to make appropriate compensatory adjustments.

The purpose of the present study was therefore:

1. to investigate in dogs the effect of thyroidectomy on catecholamine secretion during maximum oxygen consumption for a short period of exhaustive work ($Ex \, V_{O_2 \text{max}}$) and for a severe cold stress ($C_{VO_2 \text{max}}$). Under each condition
we have compared the plasma adrenaline and noradrenaline concentrations in each dog before and after thyroidectomy;

2. to monitor changes in the metabolic effect of catecholamines after thyroidectomy: glucose, FFA and lactic acid plasma concentrations which can be considered to reflect the metabolic activity of catecholamines were also measured.

**Methods**

**Material**

Experiments were carried out on adult mongrel dogs (5 females and 2 males) weighing from 9 to 13 kg. The animals were housed in a temperature controlled room at 21°C. The experiments were performed after 18 h fasting. Water was supplied ad libitum. Two weeks before the experimental period a catheter was inserted into the jugular vein to permit blood sampling during the experiments. The dogs performed the muscular exercise on a treadmill at speeds ranging from 8-13 km/h on slopes of between 8 and 20%. A metal grid delivering non noxious electrical shocks was mounted at the rear end of the treadmill and was employed as necessary to ensure that strenuous work was maintained. The dogs had been previously accustomed to run with a plastic respiratory mask suspended by springs from the ceiling. The cold tests were performed by cold immersion as previously described (Therminarias et al. 1979): the dogs were held in a hammock according to the weight of animals, in order to achieve the maximum level of exercise. The rear end of the treadmill and was employed as necessary to ensure that strenuous work was maintained. The dogs had been previously accustomed to run with a plastic respiratory mask suspended by springs from the ceiling. The cold tests were performed by cold immersion as previously described (Therminarias et al. 1979): the dogs were held in a hammock so that they were unable to move and then were abruptly immersed up to the neck in a thermostatically controlled stirred bath. A water temperature of 8-16°C was chosen, according to the weight of animals, in order to achieve the maximum level of exercise. The same respiratory mask as used for the muscular exercise experiments was placed over the animal’s head to allow measurements of O2 uptake and CO2 production. O2 uptake was determined with an open circuit system: an accurately measured air flow was maintained through the mask and air was continuously drawn from the mask and analysed for O2 (Paramagnetic analyser Magnos 3, Hartmann and Braun) and CO2 concentrations (infrared analyser ContrNe de chauffe). Oxygen, carbon dioxide values and ECG were continuously recorded. The flow rate through the mask was adjusted so that the CO2 concentration did not exceed 0,8%. Oxygen uptake was calculated according to Depocas and Hart 1957. A thermistor probe which was inserted through the anus allowed colonic temperature to be continuously recorded throughout the period of cold immersion. During muscular exercise colonic temperature was measured at the onset and at the end of each test. Before and at the end of each experiment a blood sample was taken for estimations of plasma epinephrine and norepinephrine (Da Prada and Zurcher 1976), glucose (Technicon Autoanlyser), lactate (Hohorst 1965) and FFA (Dole and Meinertz 1960). Hematocrit was also monitored. Surgical removal of the thyroid gland was performed on 7 dogs. The surgical procedure was followed 5 days later by treatment with 1 131 to destroy ectopic thyroid tissue. Completeness of the procedure was judged by excessive gain in body weight and decrease in plasma T4 level.

**Experimental Procedure**

Exhaustive runs and cold immersions were performed on the same dogs before (N dogs) and after thyroidectomy (T dogs). The results obtained before thyroidectomy have been reported in a previous study (Lucas et al. 1980), and were used as control values. Experiments were begun 4-6 weeks after thyroidectomy. Two experiments per week were carried out in a random order, the duration of each experiment was 5-15 min for exercise and 30 min for cold immersion.

During each period of cold immersion, water temperature was maintained constant. After about 10 min of immersion oxygen uptake had increased to a stable level and no further increase in oxygen uptake was attained if the immersion was continued. This level of oxygen uptake was dependent upon water temperature; over a wide range of temperature the oxygen uptake increased as water temperature was decreased and at a water temperature which was specific for each dog, the maximum value of oxygen uptake was reached. At this water temperature, the colonic temperature started to decrease after a few minutes of immersion and in order that this decrease would not exceed 4°C within 30 min we had to adjust the water temperature. Indeed, if the water temperature was too low, the colonic temperature decreased so rapidly that the maximum level of VO2 max could not be reached. For this reason we found that at least 3 immersions were necessary in order to ascertain the water temperature at which the VO2 max value was attained. Before thyroidectomy the first immersion was performed at 12°C and depending on the time course of the change in colonic temperature at this temperature, further immersions were performed at colder or warmer water temperatures. After thyroidectomy the water temperature was set at the control temperature chosen for each dog before thyroidectomy. If the fall in colonic temperature then exceeded 4°C during 30 min immersion the experiment was repeated 1 week later in warmer water.

In the exercise experiments before thyroidectomy, the speed and/or slope were progressively increased in order to reach the maximum oxygen uptake between the 10th and the 15th min of running. Heart rate was continuously monitored and the increase of the work load was adjusted accordingly. During the last 5 min the electrical grid was activated to ensure that the dog maintained maximum level of exercise. Ex VO2 max was considered to have been reached when a) no further increase in oxygen uptake was obtained despite a further increase in the work load, b) heart rate reached a maximum level, c) plasma lactate was elevated.

After thyroidectomy we had to shorten the time which served as a warming up period and maximum oxygen uptake was reached between the 5th and the 10th min of running. Ex VO2 max was considered to have been reached when no further increase in oxygen uptake was obtained despite a further increase in the work load. At least 3 exercise tests were performed on each dog in order to verify that the Ex VO2 max was reproducible. For each test, maximum oxygen uptake was determined as the peak value attained during a 1-3 min period. In each dog the highest values of O2 uptake obtained during cold immersion and during exercise were considered as the CVO2 max and the Ex VO2 max values.

**Results**

After the thyroidectomy the dogs were definitely hypothyroid as judged by low T4 plasma concentration and an increase in body weight (Table 2). Indeed 4-6 weeks after thyroidectomy all dogs showed an increase in body weight. The increase amounted is to 19 to 51% of their weight before thyroidectomy.