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Catecholamines and the Effects of Exercise, Training and Gender

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Abstract

Stress hormones, adrenaline (epinephrine) and noradrenaline (norepinephrine), are responsible for many adaptations both at rest and during exercise. Since their discovery, thousands of studies have focused on these two catecholamines and their importance in many adaptive processes to different stressors such as exer-

cise, hypoglycaemia, hypoxia and heat exposure, and these studies are now well acknowledged. In fact, since adrenaline and noradrenaline are the main hormones whose concentrations increase markedly during exercise, many researchers have worked on the effect of exercise on these amines and reported 1.5 to >20 times basal concentrations depending on exercise characteristics (e.g. duration and intensity). Similarly, several studies have shown that adrenaline and noradrenaline are involved in cardiovascular and respiratory adjustments and in substrate mobilization and utilization. Thus, many studies have focused on physical training and gender effects on catecholamine response to exercise in an effort to verify if significant differences in catecholamine responses to exercise could be partly responsible for the different performances observed between trained and untrained subjects and/or men and women. In fact, previous studies conducted in men have used different types of exercise to compare trained and untrained subjects in response to exercise at the same absolute or relative intensity. Their results were conflicting for a while.

As research progressed, parameters such as age, nutritional and emotional state have been found to influence catecholamine concentrations. As a result, most of the recent studies have taken into account all these parameters. Those studies also used very well trained subjects and/or more intense exercise, which is known to have a greater effect on catecholamine response so that differences between trained and untrained subjects are more likely to appear. Most findings then reported a higher adrenaline response to exercise in endurance-trained compared with untrained subjects in response to intense exercise at the same relative intensity as all-out exercise. This phenomenon is referred to as the 'sports adrenal medulla'. This higher capacity to secrete adrenaline was observed both in response to physical exercise and to other stimuli such as hypoglycaemia and hypoxia. For some authors, this phenomenon can partly explain the higher physical performance observed in trained compared with untrained subjects. More recently, these findings have also been reported in anaerobic-trained subjects in response to supramaximal exercise. In women, studies remain scarce; the results are more conflicting than in men and the physical training type (aerobic or anaerobic) effects on catecholamine response remain to be specified. Conversely, the works undertaken in animals are more unanimous and suggest that physical training can increase the capacity to secrete adrenaline via an increase of the adrenal gland volume and adrenaline content.

Nervous and endocrine systems are important mediators of the body's physiological adjustment to a variety of physical, environmental and behavioural stressors. Catecholamines are well known for the role they play in these adaptive processes both at rest and in response to acute stress. Under normal conditions, stress is considered as a primary factor in catecholamine secretion.[1] Indeed, a marked increase of plasma catecholamine concentrations is often observed in response to various stressors such as physical exercise,[1-8] or in response to various non-exercise-related factors such as insulin-induced hypoglycaemia[9] as well as after stimulation with hypoxia,[10,11] acidaemia,[11] glucagons[11] or caffeine.[12]

The term 'catecholamines' is composed of several components that are all derived from an amino acid, e.g. tyrosine. The principal components are adrenaline (epinephrine) and noradrenaline (norepinephrine). Their synthesis takes place at two levels: (i) sympathetic nervous fibre extremities for noradrenaline; and (ii) chromaffin cells of the adrenal medulla for both adrenaline and noradrenaline.[13,14] Therefore, noradrenaline is considered as

Table I. Main cardio-respiratory and metabolic effects of catecholamines

	Adrenoreceptors	Physiological effects	Responses
Cardiovascular and respiratory effects			
Heart			
atria and ventricles	β_1	↑ Contractility	↑ Cardiac output
sinotrial node	β_1	↑ Conduction velocity	↑ Heart rate
Arteries			
renal	α	Vasoconstriction	↓ Local blood flow
splanchnic	α	Vasoconstriction	↑ Systemic arterial pressure
skeletal muscles	β_2	Vasodilation	↑ Local blood flow ↓ Arterial pressure
Veins	α_2	Vasoconstriction	↑ Blood return to the heart ↑ Cardiac output
Lungs			
airway smooth muscles	β_2	Relaxation	Bronchodilation
Metabolic effects			
Liver	α_1 or β_2	↑ Glycogenolysis ↑ Glyconeogenesis	↑ Blood glucose
Muscle	β_2	↑ Glycogenolysis	↑ Blood lactate
	β_2	↓ Glucose utilization	↑ Blood glucose
Pancreas	α_2	↓ Insulin secretion	↑ Blood glucose
	β_2	↑ Insulin secretion	↓ Blood glucose
Adipose tissue	β_1 β_2 β_3?	↑ Lipolysis	↑ Free fatty acids
	α_2	↓ Lipolysis	↓ Free fatty acids

↓ indicates decrease; ↑ indicates increase; ? indicates not sure.

a neurotransmitter and a hormone, and adrenaline only as a hormone. Since the adrenal medulla is under sympathetic nervous system control, we often talk about the sympathoadrenal system. Therefore, noradrenaline and adrenaline are considered, respectively, as indexes of the sympathetic nervous system activity and the adrenal medulla activity.

Catecholamines act by using membrane receptors.[15] There are at least two adrenergic receptor sites (α and β). These two last receptors are also divided into subtypes α_1, α_2, β_1 and β_2[16] and β_3.[17] Noradrenaline primarily activates α-receptors and adrenaline activates primarily β-receptors, although it may also activate α-receptors (for review see Garcia-Sainz[18]). Stimulation of α-receptors is associated with constriction of small blood vessels in the bronchial mucosa and relaxation of smooth muscles of the intestinal tract. β-Receptor activation relaxes the bronchial smooth muscles, which cause the bronchi of the lungs to dilate. In addition, β-receptor stimulation also affects the heart and causes an increase in the rate and force of contractions (table I).

The activation of the sympathoadrenal system may induce several physiological effects on the body (for review see Hanoune[19]). Catecholamines have been shown to stimulate respiratory, cardiac, metabolic and thermoregulatory functions. These results were obtained by using different methods, such as the adrenal medulla ablation in animals, pharmacological sympathectomy, adrenaline and noradrenaline infusion, α- or β-blockades and marked adrenaline. Therefore, all these methods have some limits that must be taken into account when interpreting results.

Catecholamines act well simultaneously at several levels to permit the realization and/or the prolongation of physical exercise. For example, during prolonged exercise, catecholamines play a major role in oxygen and energetic substrates transportation to active muscles. Hence, studies using β-blockade report a decrease of endurance capacity and maximal oxygen uptake ($\dot{V}O_{2max}$). This decrease in performance is often explained by the action of catecholamines at the metabolic and haemodynamic levels. In fact, when using β-blockade to inhibit

catecholamine secretion, Laustiola et al.[20] reported a decrease of heart rate and blood flow pressure both at rest and in response to exercise. This inhibition also reduces $\dot{V}O_{2max}$, plasma glucose, plasma free fatty acid, plasma glycerol and blood lactate concentrations.[3] It is also demonstrated that catecholamines influence physical performances in response to maximal or supramaximal exercises by regulating muscular glycogenolysis[21] and hepatic glycogenolysis.[22-24] Therefore, it is clear that a high capacity to secrete these hormones represents an advantage in competitive sports.[1,5,25]

At rest and in response to exercise, catecholamine concentrations are influenced by several factors such as exercise characteristics, training status and gender. However, data concerning the training status and gender influence on adrenaline and noradrenaline responses to exercise at the same absolute and/or relative intensity remain conflicting. In fact, several studies concerning catecholamine concentrations in response to exercise, did not report any effects of both endurance[26] and sprint[27] training. In addition, transversal studies did not find differences between trained and untrained subjects.[28] In contrast, some studies reported higher post-exercise adrenaline concentrations in endurance-[1,29,30] and sprint-trained[4] subjects compared with untrained subjects or in anaerobic-trained subjects compared with aerobic-trained subjects.[31] Other studies also reported higher significant noradrenaline concentrations in response to exercise after endurance training[32,33] or when comparing endurance-trained subjects to untrained subjects.[30] The training effect on catecholamine responses has already been reviewed.[1] However, it can be noted that this review focused on the effect of training on adrenaline responses to exercise. In the present article, we added new data about the effect of different types of training such as endurance, sprint and strength training on both adrenaline and noradrenaline, and possible gender differences.

Gender is also a potential factor able to alter catecholamine concentrations whether at rest or in response to exercise.[34-37] However, several studies did not report any significant differences between men and women, at rest or in response to exercise.[38-40] As previously suggested by Viru,[41] some methodological differences may probably explain part of the contradictions. However, it seems also that the training status of the subjects must be taken into account when studying gender differences (as men and women may respond differently to physical training). Briefly, different training status and possibly even different levels of training may have contributed to the failure to detect gender differences in the previous studies.

In this article, we first review the effects of exercise and its characteristics on adrenaline and noradrenaline concentrations. Special attention is then given to the effect of different types of training on both adrenaline and noradrenaline concentrations measured both at rest and in response to exercise. Finally, we focus on other aspects such as the training effects on adrenal glands and adrenergic receptor density and sensitivity in men and women, but also in animals as these last parameters are not well studied in humans.

1. Exercise and Catecholamine Responses

Physical exercise can be considered as a stressor that is able to stimulate the sympathoadrenal system.[42] Nevertheless, the sympathoadrenal response to exercise varies according to certain characteristics of physical exercise. Indeed, the posture of the subject at rest or during exercise and the characteristics (type, duration and intensity) of exercise are factors that most influence the catecholamine responses.

1.1 Posture Effect

The majority of studies agree on the fact that, in untrained subjects, posture influences plasma catecholamine concentrations. At rest, the catecholamine concentrations measured in a sitting or lying position are lower than those measured in an upright position.[3,14,43-47] For Korht et al.,[47] adrenaline and noradrenaline plasma concentrations increase, on average, >40% in an upright position. In this last study, the adrenaline concentrations pass from 43 to 62 ng/L (0.23–0.34 nmol/L) and the noradrenaline concentrations from 348 to 696 ng/L (2.06–4.1 nmol/L) between the lying and the upright position.

The posture also likely influences the plasma catecholamine concentrations during exercise. Thus,

several authors observe significantly higher noradrenaline concentrations after a same intensity exercise carried out in an upright position or in a lying position.[3,43-45,48] However, it seems that physical training affects this postural adaptation since Bloom et al.[49] and McCrimmon et al.[50] do not observe any differences related to the posture between trained and untrained subjects at rest. These last results are not systematically found in all the studies.[51-55]

1.2 Exercise Type Effect

1.2.1 Exercise with Upper or Lower Body

During dynamic exercise with the same oxygen uptake ($\dot{V}O_2$), adrenaline and noradrenaline plasma concentrations are higher when the exercise is carried out with arms rather than legs.[56,57] The main explanation is that the muscular mass brought into play is lower during arm exercise. This assumption is supported by different data. By measuring heart rate and vascular resistances in the splanchnic territories, Clausen[58] reported that the sympathetic nervous stimulation as well as the ventilation were higher when the exercise was carried out with a small muscular group than with a big muscular group. Moreover, Davies et al.[56] showed that at same $\dot{V}O_2$ level the increase in adrenaline and noradrenaline plasma concentrations was significantly higher when the exercise concerned a small rather than a big muscular group. Finally, Kjær et al.[59] emphasized that, at the same absolute $\dot{V}O_2$ level, a small muscle mass is working at a relatively higher percentage of its $\dot{V}O_2$ peak than a larger muscle mass, simultaneously inducing higher catecholamine concentrations.

1.2.2 Dynamic or Static Exercise

The increase in the adrenaline and noradrenaline plasma concentrations, related to the increases in $\dot{V}O_2$ and heart rate, seems to be more important during isometric exercise than during dynamic exercise. However, all the data are not univocal probably because it is difficult to precisely compare a dynamic exercise and a static exercise. Indeed, the static exercise is accompanied by a permanent compression of the intramuscular vessels. This results in a reduction of the active muscles blood flow, which induces an additional hypoxic stress. That makes the comparison between isometric and dynamic exercises very debatable.

Plasma catecholamine concentrations are known to increase markedly in men during dynamic exercise in various sporting specialties, such as running,[3,44,60-62] cycling[5-7,39,40,43,49,63-68] and swimming,[45,69] but also during static exercises.[70,71] During dynamic exercise of short duration, there is no significant increase of plasma catecholamine concentrations if the heart rate does not increase over 30 beats/min (corresponding to approximately 30% of $\dot{V}O_{2max}$ related to body mass).[43] If the heart rate strongly increases during exercise, a marked increase in plasma concentrations of adrenaline and noradrenaline is then observed.[49,60,63,64] However, noradrenaline plasma concentration can significantly increase for work intensities lower than those necessary for a significant increase in adrenaline concentration.[60,65-72]

Isometric exercise induced a marked increase in the plasma catecholamine rates during a contraction of the quadriceps muscle (only one leg) lasting 2 minutes at 40% of the maximum force.[48] From a resting value of 0.21 ng/mL (1.24 nmol/L) noradrenaline reaches 0.32 ng/mL (1.9 nmol/L) with exercise. Adrenaline passes from 0.10 ng/mL (0.55 nmol/L) at rest to 0.24 ng/mL (1.32 nmol/L) in response to exercise.[42] Some authors reported important increases in the adrenaline and noradrenaline concentrations during the isometric exercise carried out until exhaustion.[70,73,74] For Galbo[42] and Watson et al.,[48] the increase would be comparatively stronger for adrenaline than for noradrenaline. However, these results are not found in all the studies. Thus, Robson and Fluck[75] and Watson et al.[76] did not find any change of catecholamine concentrations in response to isometric exercise. These apparently contradictory data can be explained either by the intensity of the exercises carried out or by the selected methods of dosage. On the other hand, the heart rate level reached during the static exercise suggests that the exercise intensity remains relatively low.[75,76]

When trying to compare dynamic and isometric exercise equated on duration time to exhaustion, Lewis et al.[77] showed a more significant increase in the noradrenaline concentrations during a dynamic exercise compared with a static one, whereas the

adrenaline concentrations did not differ significantly. For these authors, the results observed during isometric exercise could be explained by a dissociation of adrenaline and noradrenaline responses.[77]

1.3 Exercise Duration Effect

At the same level of submaximal dynamic exercise, the duration of the exercise also plays a considerable role in the sympathoadrenal activity. For a constant $\dot{V}O_2$, the plasma noradrenaline concentration continuously increases until exhaustion of the subject, whatever the intensity of the submaximal exercise.[3,55,60,78,79] At very low intensity, adrenaline and noradrenaline also increase, but it is important to note that noradrenaline concentration increases more quickly than that of adrenaline.[80] It is the same for sprint exercise. Moussa et al.[6] observed significantly higher catecholamine concentrations in untrained subjects at the end of 30 versus 6 seconds of ergocycle sprint at the same load. For Caillaud et al.[81] a minimal duration of exercise is necessary to induce an increase in the catecholamine concentrations, even at very high intensity (sprinting); however, other works did not confirm this hypothesis.[6,7,68] These last studies observed a significant increase in plasma adrenaline and noradrenaline concentrations at the end of a 6-second ergocycle sprint. These divergences could be explained by some methodological differences and especially the dosage and the intensity of exercise (optimal intensity pre-determined by a force/velocity test or not).

1.4 Exercise Intensity Effect

At comparable duration, the stress induced by an exercise is as high as the exercise is more intense. Therefore, it is logical that the sympathoadrenal responses are also greatly influenced by the exercise intensity. For a given type of exercise, the plasma catecholamine concentrations are very closely related to the intensity of the effort when expressed in a relative value (percentage of $\dot{V}O_{2max}$) or related to bodyweight.[49,56,60,72,82] In fact, adrenaline and noradrenaline concentrations seem to be conditioned by the relative power of the exercise.[59,83,84] For a given duration, the circulating noradrenaline concentrations increase exponentially with the intensity of the exercise.[72,85,86] Initially moderate, this increase becomes faster beyond 75% of the maximal aerobic power (MAP).[87] From a basal value of 0.2 ng/mL (1.18 nmol/L) it can reach 2–3 ng/mL (11.8–17.7 nmol/L) approximately at MAP. In adult subjects, the plasma adrenaline concentration at rest is approximately 0.10 ng/mL (0.55 nmol/L). When the duration does not exceed 20 minutes, it usually starts to rise at a power corresponding to 50% of the MAP and reaches 0.40 ng/mL (2.18 nmol/L) approximately at MAP.[60] In this way, Kjær et al.[88] observed that 60 minutes of exercise at 35% of $\dot{V}O_{2max}$ is enough to increase the plasma noradrenaline concentration and that 20 minutes of exercise at 40–50% $\dot{V}O_{2max}$ is necessary to increase the adrenaline concentration. Thus, when the duration is very important, adrenaline and noradrenaline can increase even at very low intensity.[80,88] In the same way, and more recently in cyclists and untrained men, Manetta et al.[66] observed significantly higher plasma noradrenaline concentration measured during 50 minutes of cycling exercise performed at 15% above the ventilatory threshold (VT) than when it is performed below this threshold.

The increase in catecholamine concentration is still more important for intensities higher than MAP.[4-6,8,25,40,67,68,83,84] Thus, the basal catecholamine concentrations, according to studies, can be multiplied by five to ten times and occasionally even more. These important increases were observed in physical education students who carried out an exercise at 156% or 130% of their $\dot{V}O_{2max}$,[83,89] in sedentary subjects at the end of an incremental exercise carried out until exhaustion (165% of $\dot{V}O_{2max}$)[90] or in athletes after a repetition of sprints of 3×300 m.[84] In physically active subjects carrying out a 30-second sprint on a non-motorized treadmill[91] and in men and women sprinters, endurance trained and untrained at the end of a Wingate test,[4,5,25,36,40,92] plasma concentrations were 85% and 88% higher than basal values for adrenaline and noradrenaline, respectively. Recently, in untrained male subjects, Bracken et al.[67] measured a 4- to 6-fold increase in adrenaline and noradrenaline plasma concentrations at the end of a 2-minute cycle test at a workload calculated to elicit 110% $\dot{V}O_{2max}$.

Higher concentrations (>20 times normal basal values) are reported by Ohkuwa et al.[61] following a 400-m race, or by Brooks et al.[35] after ten repeti-

tions of 6-second sprints on a non-motorized treadmill. In addition to these data, 3- to 5-fold higher values are also reported during other supramaximal exercises. This was the case for physical education students after a race at 22 km/hour against a slope of 7.5°[93] or during a maximum sprint carried out by women sprinters.[94] This was also the case following a 30-second sprint carried out by physically active men and women.[27] The large variability of these results according to the studies can be explained by three possibly associated factors: (i) the level of physical training of the subjects tested; (ii) the more or less long duration during which the exercise was maintained; and (iii) the width of the muscular mass brought into play according to whether the exercise is carried out in the field, on a treadmill or on a cycle ergometer. Finally, the time spent between the end of the exercise and the blood sample can also be a factor of variation. Thus, in the studies conducted by Nevill et al.[27] and Brooks et al.,[95] blood samples were drawn 3 and 5 minutes after the end of exercises, respectively. This delay is sufficient to remove a large part of the catecholamines. Indeed, after a short and intense exercise session, the catecholamine blood concentrations turn over quickly to their basal values.[96] One minute after the end of the exercise, the plasma adrenaline concentration would already be decreased by 35%.[1,29,86]

1.5 Effect of Exercise on Catecholamine Secretion and Clearance

The important concentrations of adrenaline and noradrenaline reported in the various studies after different exercise modalities, confirm that an intense effort is required to stimulate the sympathoadrenal system activity.[1,83,97] However, the origin of these high values is not completely explained. Several assumptions can be formulated to explain the plasma adrenaline and noradrenaline increase with exercise intensity. Among them, as in the long-duration exercise, these high values may result from combined changes in the catecholamine clearance and/or their secretion rate.[11,29,85] Nevertheless, even if adrenaline and noradrenaline values decrease, and considering the rapid rise in their concentrations, it is possible according to Kjær et al.[88] that a stimulation of the secretory mechanisms intervenes considerably in these variations. Kjær et al.[88] noted a reduction in the clearance with the relative load of work, particularly when the plasma adrenaline concentration increases >10-fold its basal value. The evolution of the catecholamine clearance during supramaximal exercise remains to be clarified. The increase in the clearance during moderate exercise can be explained, according to Sacca et al.,[98] by an increase in blood flow in the tissues that are responsible for eliminating this hormone. The fall of this clearance during intense exercise means that the adrenaline elimination decreases in the whole body. If it is proven that the catecholamine clearance is the sum of their elimination in all tissues, it can be assumed that the change in the distribution of the blood mass is responsible for the fall of the clearance level. Some tissues are known to be the basis of an important catecholamine inactivation such as the liver, or of a weak inactivation such as the skin. Other authors, by studying the adrenaline turnover during moderate exercise, have observed a significant fall in the adrenaline clearance.[99] However, the perfusion of great quantities of adrenaline can influence at the same time the clearance and the rate of secretion. It was suggested that the increase in the plasma noradrenaline concentration is due to a fall of its elimination from circulation.[82] However, Hagberg et al.,[96] while being interested in the noradrenaline kinetics during recovery, showed that the reduction rates of this hormone are not due to a variation of its elimination. Moreover, the variation of the site of the blood taking away can also influence this clearance by a reduction of this hormone elimination in the considered area.[88]

Consequently, the plasma adrenaline and noradrenaline concentrations determined during an intense exercise session are more the reflection of a higher secretion rather than a fall in their elimination or clearance. The particularly high concentrations of the catecholamine observed after short and intense exercises are undoubtedly mainly explained by a more important activity of the secretary mechanism. Indeed, several works, using an index of adrenaline and noradrenaline elimination demonstrated that the higher adrenaline and noradrenaline concentrations measured after supramaximal exercise are mainly due to a secretion mechanism.[4-6,8,25,36,40,68]

Finally, the importance of the feedback mechanisms of the hormonal response to exercise should not be forgotten. Thus, some local factors, such as osmolarity,[100] can affect the level of the active muscle that could, according to Brooks et al.,[91] take part in the sympathoadrenal activity regulation during supramaximal exercise. It seems, however, that the very fast changes of the catecholamine concentration observed at the end of this type of exercise do occur too quickly to be solely explained by this type of mechanism. It is probable that, parallel to the activation of the skeletal muscle, the direct stimulation of the driving centres of the brain (central order) will also be implied in the sympathoadrenal response to intense exercise. The intensity of the 'exercise to come' can also influence the resting concentrations of adrenaline. Kraemer et al.[101] observe that the plasma concentrations of adrenaline measured at rest increase with the intensity of the exercise, which has to be realised. Zouhal et al.[4] and Kraemer et al.[102] also reported a significant increase of adrenaline concentration just before intense exercise, but only in trained subjects.

1.6 Summary

Duration and intensity are the main factors able to alter catecholamine responses to exercise, but it seems that the intensity is probably the main factor. Thus, more and more authors[3,4,6-8,25,39,40,68,92,103,104] used sprint or prolonged sprint exercise to obtain the maximal catecholamine responses to exercise and then compared different populations. The increase in catecholamine concentrations is the most important factor during this type of exercise. Moreover, since duration is shorter, it can be assumed that this increase is more due to high secretion level than accumulation. As a result, post-exercise concentrations can better reflect the capacity to secrete adrenaline.

2. Training Effect on Catecholamine Responses and Sympathoadrenal System Adaptations

Historically, the first studies were longitudinal studies that focused on the endurance training effects on catecholamine responses. These studies compared the plasma catecholamine concentrations at rest and in response to exercise before and after endurance training.

2.1 At Rest in Humans

At rest, several studies did not observe any differences between pre- and post-training results.[26,105,106] Even later when comparing endurance-trained and untrained subjects, Lehmann and Keul[107] and Manetta et al.[66] failed to demonstrate a significant training effect on adrenaline and noradrenaline resting values. On the other hand, Kjær et al.[10,108] measured higher resting adrenaline concentrations in endurance-trained compared with untrained subjects. More recent work also reported differences between sprint-trained and untrained subjects.[4] Several authors[4,5,36,109] suggest that emotivity may explain those differences. Kraemer et al.[102] deduced that the higher values of adrenaline reported in trained weightlifters compared with untrained subjects were the result of a higher 'pre-increase' in preparation for an intense bout of physical exercise. For these authors, performing an exercise bout may represent a challenge for the trained subjects, such as before a competition. Kraemer et al.[102] took two measurements at rest, one 30 minutes before the exercise and the other immediately before. They observed that the values measured immediately before the exercise were significantly higher in trained compared with untrained subjects. Such results suggest that the trained subjects developed anticipating capacities. Among women, physical training did not seem to modify adrenaline and noradrenaline concentrations when measured at rest.[79,95,110]

2.2 In Response to Exercise in Humans

2.2.1 Aerobic Training Effect

As catecholamines control many functions that influence physical performance, many studies have focused on the physical training effects of these hormone responses to exercise. For clarity, we separated the studies carried out with men from those carried out among women.

In Men

Although the studies relating to the aerobic training effect on plasma adrenaline and noradrenaline concentrations induced by exercise are numerous,

Table II. Summary of endurance-related longitudinal studies in men and women

Study	Subjects	Training duration (wk)	Training type/frequency	$\dot{V}O_{2max}$ changes	Tests	Effect of training [A]	Effect of training [NA]
Brooks et al.[95]	7 F	10		5% ↑	30-sec sprint	↔	↔
Friedlander et al.[110]	15 F	12	1 h 75% $\dot{V}O_{2max}$ 5 × wk	25% ↑	1 h 65% initial $\dot{V}O_{2max}$ 1 h 65% relative $\dot{V}O_{2max}$	↔ ↔	↓ ↓
Greiwe et al.[33]	6 M + 3 F	10	4 × 5 min 90–100% $\dot{V}O_{2max}$ 3 × wk 30–40 min exhaustive 3 × wk	20% ↑	15 min 60% MAP 15 min 65% MAP 15 min 70% MAP 15 min 75% MAP 15 min 80% MAP 15 min 85% MAP		↔ ↑ ↑ ↑ ↑ ↑
Hartley et al.[72]	7 M	7	3-h distance running and aerobic games 3 × wk	14% ↑	8 min 42% $\dot{V}O_{2max}$ 8 min 75% $\dot{V}O_{2max}$ 5 min 98% $\dot{V}O_{2max}$	↔ ↓ ↓	↔ ↔ ↔
Lacour et al.[106]	6 M	22.5	1 h/d 80% $\dot{V}O_{2max}$ 4 × wk	14% ↑	1 h 85% $\dot{V}O_{2max}$	↓	↔
Péquignot et al.[109]	7 M	2	80% $\dot{V}O_{2max}$ 2 × wk		15 min 80% $\dot{V}O_{2max}$ 80% $\dot{V}O_{2max}$ until exhaustion	↔ ↔	↔ ↓
Winder et al.[26]	6 M	7	30–50 min/d 6 × wk	22% ↑	5 min 1483 kg/min	↓	↓
Winder et al.[53]	6 M	9	30–50 min/d 6 × wk	22% ↑	90 min 60% initial $\dot{V}O_{2max}$	↓	↓

[A] = plasma adrenaline concentration in response to the test; **F** = females; **M** = males; **MAP** = maximal aerobic power; **[NA]** = plasma noradrenaline concentration in response to the test; **$\dot{V}O_{2max}$** = maximal oxygen uptake; ↑ indicates increase; ↓ indicates decrease; ↔ indicates no change.

they remain contradictory (table II and table III). The first data from longitudinal studies are related to endurance training effects. Most observed that endurance training is accompanied by a decrease in plasma catecholamine concentration in response to exercise performed at the same absolute intensity.[26,49,53,72,109] On the other hand, for Lacour et al.,[106] these responses remained similar when subjects performed the exercise at the same relative intensity (% $\dot{V}O_{2max}$). By comparing endurance trained and untrained subjects, Lehmann et al.[28] also showed a close relationship between the relative exercise intensity and the plasma catecholamine concentration independent of physical training level of the subjects. In the same year, the study of Kjær et al.[9] reported for the first time significantly higher adrenaline concentrations in endurance-trained subjects compared with untrained subjects despite similar noradrenaline concentrations in response to an insulin perfusion. These authors then suggested that endurance-trained subjects have a higher capacity to secrete adrenaline than untrained subjects. These results were confirmed later in response to an incremental exercise.[29] In this last work, the post-exercise adrenaline concentration was significantly higher in endurance-trained than in untrained subjects even when working at the same relative intensity. In this same study, it is also important to note that the differences between trained and untrained subjects on plasma adrenaline concentrations in response to exercise increased with the intensity of the exercise.

Kjær et al.[29] then discuss 'sports adrenal medulla'. This phenomenon corresponds to a higher capacity in trained subjects to secrete adrenaline, which induces higher adrenaline concentrations in trained versus untrained subjects in response to physical exercise at the same relative intensity. Indeed, the higher plasma concentrations reported in trained subjects cannot be explained by a lower elimination rate, considering that Kjær et al.[88] have also verified this eventuality. In fact, elimination seems to be independent of physical training status and depends only on the relative exercise intensity so that in response to the same absolute exercise intensity, elimination differs between trained and untrained

Table III. Summary of endurance-related tranversal studies in men and women

Study	Gender	Subjects	$\dot{V}O_{2max}$	Tests, stressors	Trained/untrained	
					[A]	[NA]
Bloom et al.[49]	M	6 Racing cyclists	342	7 min 30% MAP	T < UT	T < UT
		6 UT	236	7 min 45% MAP	T < UT	T < UT
			MAP in Watts	7 min 60% MAP	T < UT	T < UT
				7 min 75% MAP	T < UT	T < UT
Boone et al.[111]	M	6 Endurance trained	58	4 min 70% $\dot{V}O_{2max}$	T = UT	T = UT
		6 UT	38	2 min 120% $\dot{V}O_{2max}$	T > UT	T > UT
Friedmann and Kindermann[79]	F	12 Well endurance trained	59	UT: 1 h 75% $\dot{V}O_{2max}$	T = UT	T = UT
		12 UT	51	T: 1 h 80% $\dot{V}O_{2max}$		
Jacob et al.[25]	F	7 Distance runners	63	Wingate test	T = UT	T = UT
		6 Untrained	43			
Jacob et al.[7]	M	6 MDR	65	Wingate test	T > UT	T = UT
		6 LDR	70			
		6 UT	43			
Kjaer et al.[9]	M	8 Elite endurance athletes	65	Insulin-induced	T > UT	T = UT
		8 UT	49	hypoglycaemia		
Kjaer et al.[29]	M	7 LDR + 1 LD skier	65	7 min 60% $\dot{V}O_{2max}$	T > UT	T = UT
		8 UT	47	3 min 100% $\dot{V}O_{2max}$	T > UT	T = UT
				2 min 110% $\dot{V}O_{2max}$	T > UT	T = UT
Kjaer and Galbo[11]	M	8 Elite endurance athletes	66	Glucagon injection	T > UT	T = UT
		7 UT	46	Acidaemia	T = UT	T = UT
				Hypobaric hypoxia	T > UT	T = UT
Lehmann et al.[28]	M	6 Marathon runners	66	Incremental test until	T = UT	T = UT
		6 UT	54	exhaustion		
Manetta et al.[66]	M	8 Young cyclists	65	50 min VT – 15%	T = UT	T = UT
		8 Young sedentary	45	50 min VT + 15%	T = UT	T = UT
		8 Middle-aged cyclists	50	50 min VT – 15%	T = UT	T = UT
		8 Middle-aged sedentary	32	50 min VT + 15%	T > UT	T = UT
Ohkuwa et al.[61]	M	8 LDR	73	400-m race	T = UT	T > UT
		7 Untrained		3000-m race	T = UT	T = UT
Ohkuwa et al.[62]	F	5 Handball players		400-m track race	UT > T	UT > T
		6 Distance runners		3000-m track race	UT > T	UT > T
		National level				
Silvermann and Mazzeo[30]	M	8 Young cyclists	62	Incremental test	T > UT	T > UT
		8 Young sedentary	42	45-min LT	T > UT	T > UT
		8 Middle-aged cyclists	51	Incremental test	T > UT	T > UT
		8 Middle-aged sedentary	35	45-min LT	T > UT	T > UT
		8 Old cyclists	43	Incremental test	T > UT	T > UT
		8 Old sedentary	28	45-min LT	T > UT	T > UT
Zouhal et al.[5]	M	6 Distance runners	70	Wingate test	T = UT	T = UT
		6 UT	38			

[A] = plasma adrenaline concentrations in response to the test; **F** = females; **LD** = long distance; **LDR** = long-distance runner; **LT** = lactate threshold; **M** = males; **MAP** = maximal aerobic power; **MDR** = middle-distance runner; **[NA]** = plasma noradrenaline concentrations in response to the test; **T** = trained subjects; **UT** = untrained subjects; **$\dot{V}O_{2max}$** = maximal oxygen consumption expressed in mL/min/kg; **VT** = ventilatory threshold.

subjects.[88] After physical training or in physically trained subjects, the same exercise performed at an absolute intensity corresponds to an exercise of lower relative intensity. Then, the adrenaline elimination will either be increased if the intensity of the exercise is low, or less disturbed if the intensity of the exercise is high.[1] This can perhaps explain the absence of differences between trained and untrained subjects concerning the catecholamine responses to the same absolute exercise or the absence of significant modifications of the adrenaline concentrations after physical training in the longitudinal

studies. Here it is also important to note that dosage methods used in the first studies were less precise possibly causing small differences to pass undetected.

Thereafter, Kjær and Galbo[11] confirmed the hypothesis that endurance-trained subjects have a greater capacity to secrete adrenaline in response to various stimuli, such as acidaemia, a hypobaric hypoxia or a hyperglucagonaemia. Later, works of Boone et al.[111] and of Silvermann and Mazzeo[30] also reported higher adrenaline concentrations in endurance-trained compared with untrained subjects in response to intense exercise. These last cross-sectional studies also suggest that endurance training is able to increase the subject's capacity to secrete adrenaline. However, such modifications are not reported by longitudinal studies.[53,72,106] For Kjær[1] and Kjær et al.,[29] these divergences could be explained, at least in part, by a very short duration and/or weak intensity of the physical training programme used in the longitudinal studies. They suggest that such modifications are possible only after many years of intense physical training. Recently, another work using a very intense test (Wingate test) argues in that way since it reports higher adrenaline responses in well trained endurance subjects compared with untrained subjects.[7] In that last study, it is also important to know that adrenaline concentrations measured after 15 minutes of warm-up (50% $\dot{V}O_{2max}$) performed before the Wingate test were similar in the three tested groups (middle-distance runners, long-distance runners and untrained subjects), which confirms the requirement of intense tests in order to detect differences. More recently, Manetta et al.[66] did not observe any significant differences in adrenaline and noradrenaline responses to two 50-minute cycle ergometer exercise tests, below and above (±15%) the VT between young endurance-trained cyclists (mean age 26 years) and untrained subjects (mean age 24 years). However, in the same study, plasma adrenaline responses to 50 minutes of cycling at VT + 15% were significantly higher in middle-aged trained cyclists (mean age 53 years) compared with sedentary subjects (mean age 52 years).

However, as reported by Kjær et al.,[97] the capacity to secrete adrenaline in endurance-trained subjects was not affected by a 5-week cessation of physical training, so that these authors do not exclude the existence of genetic predispositions.

Concerning the noradrenaline concentrations, it seems that the divergences are also related to the exercise intensities proposed in the studies. Older studies did not observe differences between noradrenaline concentrations of trained and untrained subjects in response to exercise of relatively low intensity.[26,106] Conversely, in more recent studies that propose more intense exercise, plasma noradrenaline concentrations appear to be significantly higher in endurance-trained compared with untrained subjects,[30,111] or after an endurance training programme.[33] For Greiwe et al.,[33] the increased noradrenaline concentrations in response to exercise at the same relative intensity observed after endurance training, can be explained by the increase in energy demand required by the concomitant increase in the absolute exercise intensity. To illustrate, these authors gave the following example: if two subjects with the same weight but different $\dot{V}O_{2max}$ values of 60 and 30 mL/min/kg, respectively, carry out an exercise with 75% of their $\dot{V}O_{2max}$, then the active muscles of the subject having the higher $\dot{V}O_{2max}$ need twice as much oxygen and have to degrade twice as many substrates. This implies a higher activation of the sympathoadrenal system resulting in a more important increase in the catecholamine concentration.[33]

In Women

The influence of physical training on the catecholamine responses to exercise is much less studied in women (tables II and III). Among nine women and after 10 weeks of endurance training, Brooks et al.[95] did not observe any significant differences concerning the catecholamine concentrations induced by a 30-second sprint on a non-motorized treadmill. However, it is important to specify that in this last study, the physical training proposed induced a very modest rise in $\dot{V}O_{2max}$ level of the subjects (+5%). Moreover, the plasma catecholamine concentrations were measured 3 minutes after the end of the exercise, a delay higher than the half-life of these amines. This delay, between the end of the exercise and the blood sample, can contribute, at least in part, to hide differences. Indeed, in the study of Zouhal et al.,[4] the adrenaline concen-

trations measured 5 minutes after the end of the exercise did not differ significantly between trained and untrained subjects, whereas those measured immediately at the end of the exercise were 2-fold higher in trained compared with untrained subjects. The work of Ohkuwa et al.[62] reported differences in the concentrations of adrenaline and noradrenaline in female subjects who were specialists in sprint, endurance or untrained in response to a 400-m sprint or a 3000-m race. However, here, methodological skews incite us to consider these results with some prudence. In this last study, adrenaline and noradrenaline concentrations were measured neither at rest nor after the warm-up, which itself is not specified. Finally, all the subjects carried out a 400-m sprint and a 3000-m race in the same day. Other studies[79,110] suggest that, in women, endurance training does not alter catecholamine concentration induced by prolonged exercise at the same relative intensity. However, in these last studies, it is noted that the subjects' physical training level and the test intensity proposed were lower than those found in studies in men, reporting a significant training effect.[29,30,33,111] As previously mentioned earlier in this section, a significant training effect is mainly observed at the end of very intense exercise and when comparing very well trained to untrained subjects.[29,30,111] The study of Jacob et al.[7] compared very well trained endurance subjects (competing at national level) to untrained subjects, and used a very severe stress test (Wingate test), but failed to demonstrate any training effect on catecholamine responses. In fact, despite a significant increase of adrenaline and noradrenaline concentrations at the end of the Wingate test, there was no significant differences concerning these hormone responses between endurance trained and untrained subjects. Thus, these authors conclude that endurance training has no effect on catecholamine response to exercise in women.

Summary

Most of the recent studies using more intense exercise as well as better trained subjects clearly showed that endurance-trained subjects exhibited higher post-exercise adrenaline concentrations in response to intense exercise. This is known as 'sports adrenal medulla' and corresponds to a higher capacity to secrete adrenaline in response to exercise.[1] In contrast to the results for men, there is no evidence of an aerobic training effect on catecholamine response to exercise in women. However, studies using more intense tests and high-level athletes are still needed to conclude objectively.

2.2.2 Anaerobic Training Effect

In Men

The anaerobic training (sprint and/or resistance training) effects on catecholamine responses to exercise are relatively less studied and remain contradictory as well (table IV and table V). Longitudinal studies failed to show any significant variations on catecholamine responses to weight training[112] or to sprint training[27] even if performances increased significantly. On the other hand, several cross-sec-

Table IV. Summary of anaerobic-related longitudinal studies in men and women

Study	Subjects	Training duration	Training type/frequency	Performance changes	Tests	Effect of training	
						[A]	[NA]
Botcazou et al.[8]	6 G	6 mo	20–80 m reps, technique, strength, 3 × wk	↑ Peak power	6-sec sprint (ergocycle)	↑	↔
Botcazou et al.[68]	6 B	6 mo	20–80 m reps, technique, strength, 3 × wk	↑ Peak power ↑ 30-m sprint	6-sec sprint (ergocycle)	↔	↔
Guezennec et al.[112]	11 M	4 mo	10 reps 70% 1RM × set, 9–12 sets per session, 3–4 × wk	Bench press: from 116 to 135 kg	6 x 8 x 70% 1RM 6 x 70% 1RM until exhaustion	↓ ↓	↔ ↔
Nevill et al.[27]	4 M + 4 W	8 wk	6–10 × 6 sec sprint, 2 × 30 sec sprint, 3–4 × wk	Peak power + 12%	30-sec sprint (ergocycle) 2 min 110% $\dot{V}O_{2max}$ (treadmill)	↔ ↔	↔ ↔

[A] = plasma adrenaline concentrations in response to the test; **B** = adolescents boys; **G** = adolescents girls; **M** = men; **[NA]** = plasma noradrenaline concentrations in response to the test; **reps** = repetitions; **RM** = repetition maximum; **strength** = strength exercise; **technique** = the technically specific exercise of running; **W** = women; $\dot{V}O_{2max}$ = maximal oxygen uptake; ↓ indicates decrease; ↑ indicates increase; ↔ indicates no change.

Table V. Summary of anaerobic-related transversal studies in men and women

Study	Gender	Subjects	Performance or level	Tests	Trained/untrained [A]	[NA]
Jacob et al.[25]	F	6 Sprint trained 6 UT	National level	Wingate test	T = UT	T = UT
Kraemer et al.[102]	M	7 Power lifters 12 UT	299 kg 156 kg 1RM leg press	Leg press until exhaustion 80% 1RM	T > UT	T > UT
Ohkuwa et al.[61]	M	8 Sprinters 7 UT	400 m: 53.3 sec	400-m track race 3000-m track race	SP > UT SP > UT	SP = UT SP = UT
Ohkuwa et al.[62]	F	5 HB players 6 Sprinters	National level National level	400-m track race 3000-m track race	HB = SP HB > SP	HB = SP HB > SP
Strobel et al.[31]	M	9 Sprinters 8 MDR	National level National level	Treadmill all-out test (2–3 min)	SP > MDR	SP > MDR
Zouhal et al.[4]	M	7 Sprinters 6 UT	National level	Wingate test	T > UT	T = UT
Zouhal et al.[5]	M	6 Sprint trained 6 UT	National level	Wingate test	T = UT	T = UT

[A] = plasma adrenaline concentration in response to the test; **F** = females; **HB** = handball; **M** = males; **MDR** = middle-distance runners; **[NA]** = plasma noradrenaline concentration in response to the test; **RM** = repetition maximum; **SP** = sprinters; **T** = trained subjects; **UT** = untrained subjects.

tional studies observed significant differences between sprint-trained and untrained subjects. First, Ohkuwa et al.[61] reported that at the end of a 400-m race, the adrenaline concentrations were 2-fold higher in the sprint-trained subjects compared with the endurance-trained or untrained subjects. Such results were also reported by Zouhal et al.,[4] using a Wingate test, and by Strobel et al.[31] also using an intense exercise. In healthy weight-trained subjects, compared with non-specialists, Kraemer et al.[102] in response to a series of leg flexions/extensions also observed significantly higher adrenaline and noradrenaline responses. Even here, differences were still found between the first longitudinal studies and transverse studies, which seem to be related to the characteristics of the physical training. Indeed, in longitudinal studies, training programmes are often relatively short and not very intense. However, as for aerobic or endurance physical training,[1,29] it seems that several years of intensive sprint, anaerobic or weight training are necessary to develop what is called the 'sports adrenal medulla'.[1,29] Moreover, it is also important to note that adrenaline responses seem to be higher in anaerobic-trained compared with aerobic-trained subjects. Zouhal et al.[5] reported that adrenaline responses to a Wingate test were higher in sprint- versus endurance-trained subjects, while untrained subjects exhibited the lowest concentrations. This result suggests that anaerobic training is more effective than aerobic training as previously reported by Strobel et al.[31] In fact, Strobel et al.[31] observed that the exercise-induced increase of adrenaline concentration was higher in anaerobic- versus aerobic-trained subjects, in response to an exhaustive race at 130% of the maximum aerobic speed (MAS). Finally, these authors also reported that noradrenaline responses were significantly higher in the sprinters, which was not the case in the study of Zouhal et al.[5] Thus, the anaerobic training effect on noradrenaline response remains undetermined. In contrast, recent results observed in adolescent boys demonstrated that 6 months of sprint training (two to three times a week) were not accompanied by an increase of catecholamine responses to short sprint exercise.[113]

In Women

Very few studies were interested in the anaerobic training effects on catecholamine response to exercise in women. Ohkuwa et al.[62] observed significantly higher catecholamine concentrations among women sprinters compared with endurance-trained women and untrained subjects in response to a 400-m track race. These differences were not reported any more in response to a 3000-m race. However, these results must be taken with caution since, in this study and the one conducted in men by the same

authors in 1984,[61] many methodological weaknesses have been noted. In this study, no details were provided about the 30-minute warm-up, and as no blood samples were drawn before the races, post-exercise catecholamine concentration remained difficult to interpret. Moreover, in a more recent study[25] using very well trained subjects, maximal adrenaline and noradrenaline concentrations were similar between the three groups of women tested (sprinters, endurance trained and untrained). These results were obtained despite the fact that the sprint-trained women tested by Jacob et al.[25] were of higher training level than those used in the study of Ohkuwa et al.[62] These latter authors reported an average speed of 6.47 m/sec for a 400-m run, which corresponded to approximately 61.8 seconds for a 400-m run; when all the sprint-trained women tested by Jacob et al.[25] have already run 400 m under 58 seconds, which corresponds to an average speed of about 6.9 m/sec.

To the best of our knowledge, only one longitudinal study focused on this topic in adults. In that study, Nevill et al.[27] proposed a sprint-training programme for women and men, but as the results did not differentiate the two populations, it is impossible to reach conclusions on the effects of training on catecholamine responses in women.

Finally, the study of Jacob et al.,[25] associated with those of Zouhal et al.,[5] strongly suggest that both endurance and sprint training has no effect on catecholamine response to exercise in adult women. In contrast, recent results observed in adolescent girls demonstrate that 6 months of sprint training (two to three times a week) were accompanied by a significant increase of catecholamine responses to short sprint exercise.[8] Thus, the effects of sprint training on exercise catecholamine responses depending on gender appear to be entirely opposite to those observed in adults. This argues in favour of a specific influence of pubertal maturation. The underlying mechanisms remain still to be clarified.

Summary

As reported in section 2.2.1 concerning aerobic training, studies conducted in anaerobic-trained males reported significantly higher adrenaline responses to intense exercise in sprint-trained subjects compared with untrained or in anaerobic-trained compared with endurance-trained subjects. The latest studies also suggest that anaerobic training can increase the capacity to secrete adrenaline more than aerobic training. In women, as previously reported in section 2.2.1 concerning aerobic training, anaerobic training does not seems to be a factor that is able to increase catecholamine response to exercise. However, as previously evocated for aerobic training, studies using more intense exercise and very highly anaerobic-trained women are still needed in order to conclude objectively.

2.3 In Animals

The studies undertaken in animals are more unanimous and suggest that physical training can increase the capacity to secrete adrenaline via an increase of the adrenal gland volume and adrenaline content. Work of Östman and Sjöstrand[114] observed that a physical training programme (15 weeks of endurance training) was associated with an increase in the adrenaline content of the adrenal glands. In the same way, Stallknecht et al.,[115,116] reported an increase of the adrenal medulla volume and adrenaline content after endurance training. These results, with others using shorter and lighter endurance treadmill training programmes,[117] suggest that endurance training is able to increase the capacity to secrete adrenaline via an adrenal medulla hypertrophy. However, in rats, no study makes it possible to specify which type of physical training (aerobic or anaerobic) has the most effects on the catecholamine response to exercise. On the other hand, it seems obvious that the more intense the exercise is, the more significant the differences are likely to appear between the various groups.

Finally, Schmidt et al.[117] observed that in females the volume of the adrenal medulla as well as its adrenaline contents can be increased by a 10-week endurance training programme (1 hour/day, 5 days/week). Stallknecht et al.[116] also observed an increase in adrenal medulla volume and adrenaline contents in female rats at the end of a 10-week endurance training programme. However, as noticed by Kjær,[1] in the study of Stallknecht et al.,[116] the modifications were less important in females compared with males. Concerning the females, the increase in the adrenal medulla volume was about 30%, whereas it reached 100% in males. Schmidt

et al.[117] specify that physical training can involve modifications of adrenal medulla volume and its adrenaline contents in both sexes, but would be always less important in females.

2.4 Training Effect on Adrenergic Receptors

Adrenergic receptors, also called adrenoreceptors, are found in many different types of tissues and they generate different cellular responses to catecholamines (for review see Garcia-Sainz[18]).

In response to exercise, several studies demonstrated that catecholamines play a major role in energetic substrates mobilization from the liver, from the skeletal muscle and from the adipose tissue.[3,21-24] On the other hand, catecholamines are known to stimulate cardiovascular function to favourite energetic substrates and oxygen transport to active muscles both at rest and during exercise. Consequently, physical training may influence adrenergic receptors at the level of the liver, the skeletal muscle and adipose tissue.

2.4.1 Skeletal Muscle

In endurance-trained rats, a positive correlation was found between skeletal muscle oxidative capacity and β-adrenoreceptor density.[118-120] In the same way, endurance training adaptations are inhibited by β-blockers in humans[121] and in rats.[122] In contrast, during long bed rest, deconditioning is attenuated when subjects use β-agonists.[123] Several studies showed an increase of β-adrenoreceptor density in response to endurance training in animals.[118,120,124] This increase of β-adrenoreceptor density may lead to a higher muscular and hepatic glycogenolysis stimulation.

On the other hand, this adaptation was shown in type I and type IIa fibres, the primarily solicited fibres during endurance training.[118,119,124] Williams et al.[118] observed a higher increase of β-adrenergic receptor density in the soleus (muscle composed of 87% type I fibres) than in the gastrocnemius (mixed muscle) after 10 weeks of endurance training in rats. This result was confirmed by other studies also conducted in rats after an aerobic training programme.[120,124] However, other studies failed to show the same results in humans[119] as in animals.[125] These divergences might be explained by methodological differences such as training intensity and duration, and the type of muscle considered.

If endurance training is often accompanied by an increase of β-adrenergic receptor density, their sensitivity remains unchanged.[118,119,124,125]

Consequently, endurance training may modify the β-adrenoreceptor density, which can favour the oxidative metabolism. Nevertheless, anaerobic training effects on adrenoreceptor adaptations remain unknown. To the best of our knowledge, only one study[126] reported no differences in β-adrenergic receptor density between weightlifters and sedentary subjects.

2.4.2 Adipose Tissue

Catecholamines are known to play a major role in lipid metabolism.[127] In fact, the activation of β_1-adrenoreceptors localized in adipose cell tissue stimulates the triglyceride lipase, which is responsible for triglyceride hydrolysis. Hence, free fatty acid efflux is facilitated by vasodilatation induced by the stimulation of β-adrenergic receptors localized in local blood vessels. Physical training increases sensitivity to adrenaline and noradrenaline of β-receptor-mediated lipolysis in fat cells without increasing the number of receptors.[125] In humans, endurance training is shown to be accompanied by an increase of β-adrenergic receptor sensitivity in adipose tissue.[128] In endurance-trained women, the adrenergic lypolytic properties were higher than in sedentary women. In fact, in endurance-trained women, β-adrenergic receptor sensitivity was enhanced, whereas α_2 receptor (anti-lypolytic role) sensitivity was diminished.[129] No data are available concerning anaerobic training effects on β-adrenergic receptors in adipose tissue.

2.4.3 Heart Muscle

Beneficial effects of endurance training on cardiovascular capacity are well documented (for review see Libonati[130]). Adaptations occurred at morphological and functional levels and some other adaptations were mediated by adrenoreceptor modifications. Nevertheless, studies conducted in animals show contradictory results. In fact, in response to endurance training when some studies reported no modification of β-adrenergic receptor density[118,131-133] other studies showed a decrease of this density.[134-136] Only one study[137] reported an in-

crease of β-adrenergic receptor density in rats after swim training. More recently Barbier et al.[138] reported in endurance-trained rats a decrease of β_1, no modification of β_2 and an increase of β_3 heart adrenoreceptor density. These divergences can be explained, at least in part, by experimental protocol differences as animal species, the type of tissue studied and/or the type (running or swimming), duration and the intensity of training.

In humans, the results are drawn essentially from indirect measures (blood cells, lymphocyte) and the reported data are also divergent. When Jost et al.[139] observed a decrease of β-adrenergic receptor density, Williams et al.[140] observed no modification.

To the best of our knowledge, anaerobic training effects on heart adrenergic receptor density and/or sensitivity are not yet studied.

2.5 Summary

Both aerobic- and anaerobic-trained subjects exhibited higher adrenaline response to intense exercise at the same relative intensity or to sprint exercise. This is not reported in longitudinal studies before and after training. For Kjær et al.,[9] this can be explained by the short duration and the weak intensity of the physical training. The same authors[97] did not exclude the existence of genetic predispositions in well trained endurance subjects. Such results are not reported in women, suggesting that training has no effect on catecholamine response to exercise.

As previously mentioned in the introductory section, adrenaline and noradrenaline act via receptors so that receptor density and sensitivity modifications may influence adrenaline and noradrenaline actions. However, no studies reported significantly lower density or sensitivity after training (all the studies reported either an increase or no modification) so as a result we can assume that the higher adrenaline responses to exercise are not counterbalanced by downregulation processes. Higher adrenaline responses associated with higher or unmodified adrenoreceptor density and/or sensitivity may then contribute to explain the higher performances observed in trained subjects.

In animals, studies are more unanimous and suggest that endurance training causes hypertrophy of the adrenal gland and its adrenaline content both in males and females.

3. Gender Effect on Catecholamine Responses

To better investigate the specific effect of gender, it appears necessary to compare the catecholamine responses in men and women in the same study and using the same protocol, which was never the case in the studies previously reported.

3.1 At Rest

At rest, some studies observed similar basal adrenaline and noradrenaline concentrations in men and women,[38,73,104] while others measured significantly higher concentrations in men.[35,36] Most of the time, differences were observed immediately before the test and can be related to a higher psychological stress in men for whom the realization of a test represents a challenge.[34] But other factors may be also incriminated such as differences in body composition (e.g. higher fat mass in women) and/or in sexual hormonal status.

3.2 In Response to Exercise

Physical exercise is accompanied by an increase in adrenaline and noradrenaline concentrations in women and men.[42,141] The amplitude of the increase, however, does not achieve unanimity. There are mainly two types of studies: (i) those that do not report gender differences; and (ii) those that observe significantly higher catecholamine concentrations in men than in women. Many studies[38,73,141,142] found no differences between the catecholamine concentrations of untrained or physically active men and women in response to submaximal exercise. Friedmann and Kindermann[79] observed the same results independent of the subject's physical training levels. Indeed, these authors did not observe any differences between the catecholamine concentration kinetics of untrained or endurance-trained men and women during a 10–17 km test on a treadmill (75% or 80% of their $\dot{V}O_{2max}$). Friedlander et al.[110] observed no differences between the catecholamine responses of untrained men and women, in response to 1 hour of cycling (65% of their $\dot{V}O_{2max}$). In response to a more intense exercise (Wingate test),

Zouhal et al.[39] also found no gender differences in the adrenaline and noradrenaline responses of highly endurance-trained men and women paired on their level of $\dot{V}O_{2max}$ (related to lean body mass) and on their level of competition. Accordingly, and considering the response to very intense exercises of legs flexion/extension using various intensities and until exhaustion, Pullinen et al.[104] did not note differences between physically active men and women.

Other studies observed different catecholamine responses to exercise between men and women. In physically active subjects, Brooks et al.[35] observed significantly higher plasma adrenaline concentrations in men compared with women in response to a set of ten 6-second sprints on a non-motorized treadmill. In the same way, in sprint-trained men and women paired according to their level of competition, Gratas-Delamarche et al.[36] reported 2-fold higher adrenaline concentrations in men compared with women in response to the Wingate test. After 12 weeks of endurance training (1 hour/day of cycling at 75% of $\dot{V}O_{2max}$, 5 days/week), Friedlander et al.[110] observed that adrenaline and noradrenaline concentrations were significantly higher in men in response to 1 hour of cycling at 65% of $\dot{V}O_{2max}$. In untrained men and women, Horton et al.[80] reported higher catecholamine concentrations in men during a very low-intensity test (40% of $\dot{V}O_{2max}$), but of important duration (2 hours). Carter et al.[143] concluded also that after an endurance training programme men exhibited significantly higher adrenaline concentrations than women at the end of a prolonged moderate exercise (90 minutes at 60% of $\dot{V}O_{2max}$). Finally, we noticed that Lehmann et al.[144] found much higher adrenaline and noradrenaline responses among women compared with men. In this study, the authors compared the adrenaline and noradrenaline responses of men and women subjects having the same MAS at the end of an incremental treadmill exercise until exhaustion.

As Viru[41] underlined, much of these divergences can be explained, at least in part, by the diversity of the protocols used in the studies. All of the studies that focused on gender effects on catecholamine responses to exercise used:

- subjects of different ages;
- subjects of different physical training levels and different sporting specialties;
- different blood sampling times;
- different dosage methods;
- different exercise nature;
- significant varying intensities and durations.

Moreover, in many studies, the physical training levels and the status of the subject as well as the warm-up, which precedes the exercise, are needed to be briefly described. Finally, among women, the phase of the menstrual cycle is rarely specified. Most of these factors are known to influence the plasma catecholamine concentrations measured whether at rest or during exercise and must be taken into account.[8]

Thus, when taking into account most of the parameters able to affect adrenaline and noradrenaline responses,[5,25] two recent studies conducted in highly trained men and women using the same test (Wingate test) reported no training effect on catecholamine responses in women, but significant differences between untrained and trained men (sprinters and endurance trained).

3.3 Summary

There is no evidence for significant differences between men and women concerning catecholamine responses to exercise in untrained subjects. However, in endurance- and sprint-trained subjects, men exhibited significantly higher adrenaline responses to exercise than women. This might be due, at least in part, to differences of physical training type, intensity and/or duration.

4. Other Factors Affecting Catecholamine Responses

4.1 Age Effect

At rest, plasma noradrenaline concentration increases with age, while the concentration of adrenaline does not seem to be affected.[30,42,66,145,146] According to Mazzeo et al.,[147,148] these various results could be explained either by an increase in the sympathetic nervous activity with advancing age, or by a compensatory mechanism related to the fall of the organization sensitivity to sympathoadrenal stimulation. To explain the aging effects on the

resting adrenaline and noradrenaline concentrations, various authors studied the clearance of these hormones using a marked adrenaline or noradrenaline infusion.[145,146,149] For Young et al.,[149] Hoeldtke and Cilmi[145] and Morrow et al.,[146] the noradrenaline clearance decreases with aging. Thus, this factor could explain the age-related increase in plasma noradrenaline concentrations at rest, at least partially. For adrenaline, the clearance does not seem to vary with advancing age.[146] Thus, it is more difficult to explain the reduction in basal adrenaline concentrations with the age.

The data concerning the advancing age effects on catecholamine responses to exercise are very few and not univocal. For example, in response to maximal exercise, Lehmann et al.[150] observed significantly lower plasma adrenaline concentrations in older subjects compared with younger ones for similar noradrenaline concentrations. In response to a supramaximal exercise, Zouhal et al.[151] observed significantly lower adrenaline concentrations in response to exercise in 34-year-old subjects compared with younger ones, despite the fact that noradrenaline concentrations were significantly higher in the older subjects. This reduction in the adrenaline responses to physical exercise with advancing age can be explained by a fall in the adrenal medulla glands sensitivity to sympathetic nervous stimulation and/or by an atrophy of the adrenal medulla glands.[151]

In men, the noradrenaline responses to isometric exercise were positively correlated with age.[152] It seems that these changes related to aging are not due to deteriorations in the noradrenaline disappearance, since the clearance of this hormone measured at rest (lying position) does not change with aging.[149] On the other hand, the catecholamine clearance during exercise can vary. Using a noradrenaline infusion, Morrow et al.[146] observed a fall in noradrenaline clearance associated with an increase in its appearance rate in circulation with advancing age. This report is confirmed by the data of Hoeldtke and Cilmi,[145] which advance that the noradrenaline appearance speed in the circulation increases with aging. The authors suggest a deterioration of the sympathetic nervous system local operation.

Physical practice seems to be able to partially counteract these aging effects on catecholamine responses to exercise. Silvermann and Mazzeo[30] observed similar catecholamine responses in older endurance-trained subjects (average age of 65.5 years) and in untrained younger subjects (average age of 22.9 years). However, more recently, Zouhal et al.[151] observed a deterioration of catecholamine responses as soon as the fourth decade despite a high level of training of the subjects. These authors measured lower adrenaline concentrations in the 34-year age group compared with the 21-year age group at the end of the Wingate test. In that study, the two groups were matched for their endurance training level (training quantity and competition level). In the same way, Manetta et al.[66] observed that plasma noradrenaline responses to 50-minute cycle ergometer exercise performed above the VT (±15%) were significantly higher in middle-aged trained cyclists (mean age 53 years) compared with young trained cyclists (mean age 24 years).

4.2 Emotional State Influence and Test Habituation

Catecholamines are qualified hormones of stress. Consequently, any stressing situation may induce an increase in their secretion.[34,153] When an experiment is taking place, the fact of being surrounded by medical personnel in a non-familiar place, to carry out a physical exercise and to undergo blood sampling constitute an important source of stress for the subjects. Consequently, the adrenaline and noradrenaline basal concentration measurements should be made at the end of a certain resting period.[109] Despite these precautions, some subjects are qualified as emotional persons (noradrenaline/adrenaline ratio <1) or as non-emotional persons (noradrenaline/adrenaline ratio >1).[109]

Finally, the subjects' habituation in the realization of the test conditions represents another important point to consider. Péquignot et al.[109] noticed a fall of adrenaline concentration and an increase in noradrenaline concentration in response to the same exercise by the same subject on three different days. Comparable results were reported in the rat by Scheurink et al.[22] These authors suggest that the familiarization with the conditions of the test can directly influence adrenaline and noradrenaline concentrations at rest as in response to exercise.

4.3 Nutrition Status Effect

Catecholamines are known to influence the energy substrates mobilization and use at rest and in response to exercise. Studies were then interested in the influence of nutritional state on catecholamine responses. Two important points were discovered:
1. Fasting on the day of the test directly influences the catecholamine concentrations both at rest and in response to exercise.[154] In this study, five subjects underwent, twice, a cycling exercise at 80% of $\dot{V}O_{2max}$ until exhaustion, either after 15 hours of fasting or 2 hours after a light meal. The first situation generated significantly higher catecholamine concentrations at rest and in response to the exercise than did the second situation.
2. The use of various diets is also known to induce significant modifications on substrate use. However, such modifications do not seem to directly influence the catecholamine responses to exercise. Following 3 days of a low-carbohydrate diet (<5%), Langfort et al.[155] observed significantly higher adrenaline and noradrenaline concentrations at rest, but not in response to physical exercise. Following similar methodology, Lavoie et al.[89] did not report any effect of a low-carbohydrate diet on adrenaline and noradrenaline concentrations measured both at rest and in response to very intense exercise (1 minute, 30 seconds at 130% of $\dot{V}O_{2max}$). Such results suggest that the diet did not significantly influence the concentrations in adrenaline and noradrenaline in response to exercise.

4.4 Other Factors

Other factors are also likely influence the catecholamine responses. Some pathologies such as arterial hypertension, hyperthyroidism or some disturbances of the autonomous nervous system are associated with modifications of catecholamine responses.

Caffeine intake is also known to induce an increase in catecholamine concentrations.[156] In response to the Wingate test, these authors observed that caffeine intake increases adrenaline and noradrenaline responses.

Percentage body fat has also been reported to be a possible factor able to influence catecholamine responses both at rest and in response to a stimulus such as physical activity. Several authors reported significantly lower adrenaline concentrations in obese people both at rest and in response to different stimuli (for review see Young and Macdonald[157]). Endurance training has been shown to improve the sensitivity of adipose tissue of catecholamines so that the exercise-lipolysis level simultaneously increases.[158,159]

5. Conclusion

Among the many numerous factors able to influence the catecholamine response at rest or during exercise (emotivity, nutritional status, posture), exercise intensity, training intensity, gender and likely the pubertal maturation in the young appear to play a major role. Indeed, the highest catecholamine concentrations were measured in response to very intense exercise and were reached by very highly trained sprinters or middle-distance runners rather than long-distance runners or untrained subjects. The works undertaken in animals suggest that physical training can increase the capacity to secrete adrenaline via an increase of the adrenal gland volume and adrenaline content. This phenomenon is called the ‘sports adrenal medulla’. However, this particular training effect is not systematically found in women, since most of the studies did not observe any significant effect of training in women.

Finally, very recent data demonstrate that the training effect on catecholamine response, depending on gender, is entirely different during puberty, which reinforces the fact that differences in sex steroid hormones play a major role in exercise-catecholamine responses. Further investigations are needed to clarify this point.

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