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Review Article

Blood Pressure Control at Rest and during Exercise in Obese Children and Adults

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The hemodynamic responses to exercise have been studied to a great extent over the past decades, and an exaggerated blood pressure response during an acute exercise bout has been considered as an indicator of cardiovascular risk. Obesity is a major factor influencing the blood pressure response to exercise since evidence indicates that the arterial pressure response to exercise is exacerbated in obese compared with lean adults. Signs of augmented responses (such as an exaggerated blood pressure response) to physical exertion appear early in life (from the prepubertal years) in obese individuals. Understanding the mechanisms that drive the altered hemodynamic responses during exercise in obese individuals and prevent the progression to hypertension is vitally important. This paper focuses on the evidence linking obesity with alterations of the autonomic nervous system and discusses the potential mechanisms and consequences of the altered sympathetic nervous system behavior in obese individuals at rest and during exercise. Furthermore, this paper presents the alterations in the reflex regulatory mechanisms ("exercise pressor reflex" and baroreflex) in obese children and adults and addresses the effects of training on obesity-related disturbances.

1. Introduction

The hemodynamic responses to exercise have been extensively studied over the past decades. An exaggerated blood pressure response during an acute dynamic exercise bout (defined as an increase in systolic blood pressure from rest of >10 mmHg per metabolic equivalent or a diastolic blood pressure change of >10 mmHg at any workload) [1] has been considered as an indicator of cardiovascular risk [2–6]. Miyai et al. [7] showed a significant and independent threefold higher risk for future hypertension in middle-aged normotensive men with a disproportionate exercise response. A consistent relationship between resting blood pressure and blood pressure decline during postexercise recovery has also been reported [8–10]. Factors that have been accounted to influence the arterial pressure responses to exercise include resting arterial pressure levels, age, gender, ethnicity, family history of hypertension, and other genetic factors, hyperlipidemia, and obesity and physical fitness levels [11–13]. In fact, obesity is a major factor influencing the blood pressure response to exercise since evidence indicates that the arterial pressure response to exercise is exacerbated in obese compared with lean adults. Signs of altered responses to physical exertion, such as augmented blood pressure response or a chronotropic incompetence appear early in life (from the prepubertal years) in obese individuals [14, 15]. Understanding the mechanisms that drive the altered hemodynamic responses during exercise in obese individuals and prevent the progression to hypertension is vitally important.

The present paper will focus on the evidence linking obesity with alterations of the autonomic nervous system and discuss the potential mechanisms and consequences of the altered sympathetic nervous system (SNS) behavior in obese individuals at rest and during exercise. First, the mechanisms and reflexes mediating the blood pressure responses to exercise will be introduced. Next, the SNS behavior in obese individuals at rest and the consequences of alterations in SNS behavior to the blood pressure response during exercise will

be presented. Alterations in the reflex regulatory mechanisms (such as the "exercise pressor reflex" and baroreflex) in obese children and adults will also be addressed. Finally, we will conclude with studies examining the effects of training on these obesity-related disturbances and future research recommendations.

2. Mechanisms Mediating Blood Pressure Responses to Exercise

Neural control of the circulation during exercise is a multifactorial phenomenon involving higher brain centers and peripheral reflexes (Figure 1). During exercise, descending signals from a network of higher cerebral regions, from the caudal diencephalon to the rostral mesencephalon, including the ventral tegmental area [16, 17] (termed as "central command"), result in parasympathetic and sympathetic adjustments [18]. In addition, neural signals from peripheral afferents originating from the arterial baroreceptors (termed as "arterial baroreflex") [19] and from the skeletal muscle [20, 21], result in changes in the autonomic outflow. This system mediates the characteristic adjustments to exercise by controlling heart rate, stroke volume, vascular resistance, and thereby, maintaining blood pressure [22, 23].

Central command has been defined as a "feedforward" mechanism capable of activating simultaneously two separate networks, the *motor* and the *cardiovascular* control center. Central command is very important at the onset of exercise for initiating a basal level of autonomic activity and can be dictated, at least partially, by the individual's perception of effort [24, 25]. Central command plays an important role in the resetting of arterial baroreflex during exercise [26]. This effect appears to be mediated via vagal withdrawal coupled to the increase in exercise intensity.

On the other hand, "feedback" mechanisms, consisting of receptors within the exercising muscle, activate afferent nerves, and induce circulatory and respiratory adjustments to provide sufficient blood flow and remove the metabolic byproducts of the working muscle. This neural mechanism arising from the mechanical and chemical receptors within the muscle is termed the "exercise pressor reflex" [18, 21, 27]. The mechanical receptors are composed mainly by group III afferents which discharge early at the onset of contraction (mechanoreflex), whereas the metabolic receptors are composed mainly by group IV afferents that discharge later (with a latency of 5–60 seconds) with the accumulation of metabolites.

Bradykinin, K^+, arachidonic acid, analogues of ATP, diprotonated phosphate, and prostaglandins are some of the substances that have been reported to activate the nerve endings in the skeletal muscle and blood vessels [20, 21, 28]. Lactic acid has also been considered as a metabolic stimulus to group IV muscle afferents [29, 30]. Injection of lactic acid into the skeletal muscle artery has been shown to evoke reflex increases in arterial pressure that mimic those occurring during static exercise, whereas, injection of sodium lactate at a neutral pH failed to evoke a similar effect [31]. However, the demonstration that lactic acid elicits an exercise pressor reflex has been difficult since its receptor on thin

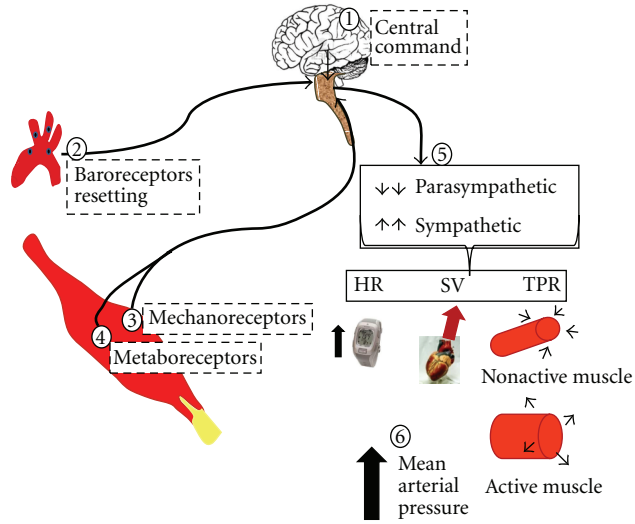

Figure 1: During exercise, neural signals originating from higher cerebral regions (1) and peripheral afferents from arterial baroreceptors (2) and the skeletal muscle ("exercise pressor reflex", 3 & 4) result in parasympathetic and sympathetic adjustments (5). Consequently, mean arterial pressure rises (6). HR: Heart Rate; SV: Stroke Volume; TPR: Total Peripheral Resistance.

afferents (group II and IV) has not been clearly identified. Recently, a direct effect of protons (H^+) on the muscle receptor itself has been suggested [32] and the acid sensing ion channel (ASIC) was shown to play a role in evoking the metabolic component of the exercise pressor reflex [33]. The hemodynamic consequence of mechanometaboreflex activation is a rise in mean arterial blood pressure [21].

Alterations in the reflex regulatory mechanisms of arterial pressure and sympathetic system disturbances have been reported in obese individuals and have been associated with the increased prevalence of hypertension and cardiovascular disorders in obesity. The mechanisms underlying the altered blood pressure responses in obese individuals have not been completely identified. Methodological refinements in the assessment of sympathetic autonomic drive throughout the years have allowed a better understanding of the role of the sympathetic nervous system in the development of obesity-induced hypertension.

3. Methods of Assessing Autonomic Nervous System Behavior

Over the years, different methodological approaches have been used to study the autonomic system behavior in obese individuals. The techniques currently applied for studying sympathetic activity in humans are (i) regional norepinephrine spillover, which measures the amount of norepinephrine released from sympathetic terminals from the coronary sinus or the renal veins using a radiotracer infusion, such as tritiated norepinephrine, and sampling of blood from the venous drainages of interest, using a central venous catheter, (ii) clinical microneurography, which measures postganglionic sympathetic nerve firing rates, bursts, in

subcutaneous nerves either of skin or skeletal muscle [34], (iii) several types of radio scanning imaging (such as positron emission tomography and single photon emission scanning), and (iv) indirect hemodynamic techniques, using blood pressure and heart rate in the assessment of sympathetic and vagal activity (such as heart rate variability, blood pressure variability, and baroreflex sensitivity measures). The first two methods described, that is, the isotope dilution methodology and sympathetic nerve recording techniques, quantify neurotransmitter release and are considered gold standards for assessing regional sympathetic nervous function in humans [35]. Skeletal muscle sympathetic nerve activity (MSNA) provides valuable information on sympathetic nerve activity at the muscle level and is an online dynamic assessment, which is highly reproducible in humans. However, MSNA does not give access to the sympathetic nerves of internal organs as the rate of spillover of norepinephrine. Ideally, combining measures of cardiac norepinephrine spillover with electrical activity of the cardiac sympathetic nerves would have yielded very conclusive evidence. However, since both techniques are invasive, simultaneous experimentation is very difficult and the information provided is restricted to laboratory environment. Therefore, other noninvasive techniques such as analysis of heart rate variability (based on mathematical models of variations in heart rate) are also available to determine the balance between cardiac sympathetic and vagal activity. Although these noninvasive methods have a number of methodological limitations that should be considered, as described by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [36], they can be employed complementary to the other methods or in studies involving healthy participants (including children). Recent advantages in heart rate variability calculation methods, such as geometrical and graphical representation (as the Poincaré plot) [37] are gaining increasing interest and can be used during exercise, since they do not require stationarity of data that was required in the time domain analysis of heart rate variability.

4. Sympathetic Nervous System Behavior in Obese Individuals at Rest: Sympathetic Underactivity versus Sympathetic Overactivity

Until recently, the relationship between obesity and SNS behavior has been controversial, since a number of studies suggested that low SNS was causal in the development of obesity [38, 39], while others, claimed that obesity was associated with high SNS behavior [40]. The reasons for these discrepancies include methods of SNS assessment as well as, the target organ examined, as SNS activity demonstrates regional specificity and thus, SNS outflow to one organ may not be similar to SNS outflow targeting other organs.

In individuals with obesity, whole body norepinephrine spillover rate (an indication of an overall sympathetic activity) has been reported similar to that in lean individuals [41, 42]. However, studies assessing cardiac SNS activity by the cardiac norepinephrine spillover rate have reported lower spillover rate (by approximately 50%) at the heart level in obese adults compared with nonobese normotensive adults, whereas renal SNS activity has been reported higher (double spillover rate of norepinephrine) in obese compared with their nonobese normotensive counterparts [41, 42]. Reduced norepinephrine spillover has been also suggested in white adipose tissue of obese individuals [43].

Direct recordings of efferent postganglionic muscle sympathetic nerve traffic via microneurography (muscle MSNA) have conclusively documented that obese individuals exhibit a noticeable increase (by as much as a twofold increase) in MSNA compared with nonobese adults during rest [44]. Visceral fat, independently of total body fat was correlated with increased basal MSNA, linking the altered SNS response with body fat distribution [45, 46]. Increased visceral fat and elevated MSNA have also been implicated in the development of obstructive sleep apnea in obese adults [47–51].

Potential mechanisms for the increased SNS activity in obese individuals include hyperinsulinemia [52, 53], hyperleptinemia [34], activation of the renin-angiotensin-aldosterone system [54–56], and mitochondrial dysfunction [57, 58]. Altered neurohumoral signals arising from the hypothalamic pituitary adrenal axis, as well as increased adipokines (adiponectin, ghrelin) [49], and dyslipidemia [59], can also be contributing factors to the observed SNS disturbances [34, 60, 61]. The "neurogenic" hypothesis of obesity has been previously reviewed [42, 59, 62]. Therefore, in this brief review we will next discuss recent findings on the alterations of reflexes controlling the blood pressure response during exercise in obese humans.

5. Sympathetic Nervous System Behavior in Obese Individuals during Exercise

In obese individuals, skeletal muscle sympathetic nerve hyperactivity is evident at rest [63]; however, during physiological stimuli, a reduced SNS responsiveness has been observed [64]. During sympathoexcitation induced by a cold pressor test, forearm vascular resistance (assessed by venous occlusion plethysmography) has been reported significantly higher in obese women compared with lean women; however, blood pressure and heart rate (monitored noninvasively by finger photoplethysmography on a beat by beat basis) similarly increased in obese and lean individuals [65]. Although in the latter study MSNA was higher in the obese than the lean group, the magnitude of the MSNA response was similar between the two groups. Negrão et al. [64] showed that normotensive obese women had enhanced resting MSNA and lower forearm blood flow than lean women [65]. During isometric handgrip exercise at 10% of the maximum voluntary contraction (MVC), when central command and mechanoreceptors are the main contributors to pressure response, the MSNA adaptation to exercise was found to be similar in obese and in lean individuals, although the absolute levels of MSNA were found higher in obese individuals. However, during 30% MVC, when central command, mechanoreceptors, and metaboreceptors are activated, the MSNA exercise adaptation was found to be blunted

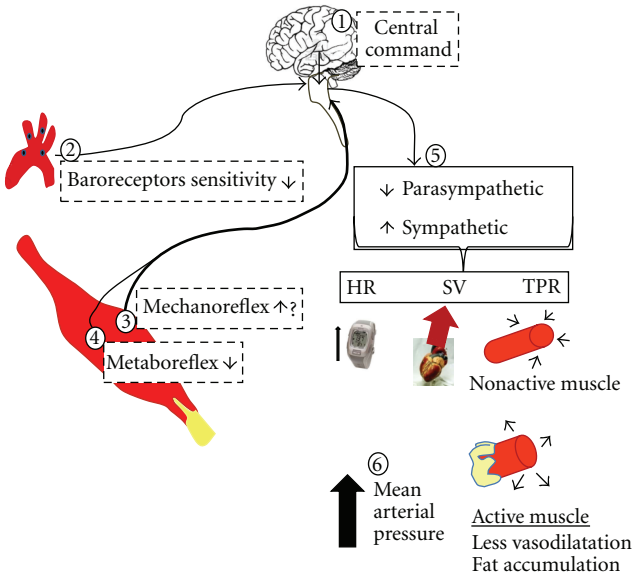

Figure 2: Alterations in the control of blood pressure during exercise in obese individuals: the baroreflex is less sensitive to stimulation (i.e., exercise) and the metaboreflex is blunted. Mechanically sensitive afferent neurons may therefore undergo functional changes to compensate for the reduced metaboreflex. These alterations may promote chronic adjustments in peripheral vascular resistance, precipitate fatigue during exercise and delay vasodilatation during exercise recovery. HR: Heart Rate; SV: Stroke Volume; TPR: Total Peripheral Resistance.

in obese women, suggesting that selective activation of metaboreceptors during exercise is impaired in obese females. This view was further explored by isolating the metaboreflex response by postexercise occlusion. During posthandgrip circulatory arrest, when the mechanoreflex and the central command are no longer active, the MSNA responses were blunted in normotensive middle-aged obese compared with lean females [64]. These findings imply that mechanically sensitive afferent neurons may undergo functional changes to compensate for the reduced metaboreflex and result in an increase in mean arterial pressure. During exercise of higher intensity, the mechanoreflex may not be able to compensate for the blunted metaboreflex, muscle perfusion might be impaired, and fatigue may appear earlier. In fact, blunted muscle perfusion to local dynamic exercise has been reported in obese individuals [66]. A proposed model for the altered exercise pressor reflex in obese individuals is presented in Figure 2.

The mechanisms underlying the blunted metaboreflex control in obese individuals are not entirely clear. Possibly, the increased fat content in the skeletal muscle in obese individuals leads to a desensitization of metaboreceptors. The reduced skeletal muscle glucose uptake observed in obesity [67] can also result in an attenuated level of acidosis in the muscle during exercise, and thus, a lower activation of metaboreceptors. A baroreflex involvement can also be implicated to this dysfunction.

Alterations in the arterial baroreflex are linked to SNS hyperactivity and blunted arterial distensibility [68, 69]. Reduced postexercise baroreceptor sensitivity and impaired autonomic regulation have been associated with an attenuated recovery of heart rate and total peripheral resistance following brisk walking in middle-aged obese women [10]. In a recent study, Fardin et al. [70] showed that baroreceptor dysfunction in obese rats (exposed to a high-fat diet) was associated with renal SNS hyperactivity. Whether this finding extend to obese humans remains to be investigated.

Preserved blood flow (assessed by Doppler) during dynamic steady-state forearm (20 contractions/min at 4, 8, and 12 kg) and leg (40 kicks/min at 7 and 14 W) exercise was found in the exercising limb in obese young healthy adults, indicating that steady-state levels of flow can be maintained via compensatory mechanisms [71]. However, in another study [72], a marked impairment in rapid vasodilatation was evident in the immediate postexercise period in obese adults and was greater with increasing workloads (from 20–50% of MVC). Differences in the reported results regarding blood flow during exercise in obese individuals could be attributed to the exercise intensity applied (similar absolute versus similar relative workload) [72], the mode of exercise (dynamic versus isometric), and the hormonal and metabolic profile of the participants (healthy versus hyperinsulinemic). The exact mechanism for the reduced postexercise vasodilatation and the delayed decline in blood pressure in obese humans is not clear. However, impaired potassium channel-mediated vasodilatation has been reported in the skeletal muscle of obese Zucker rats or hamsters [73, 74] and could be partially involved in humans.

Signs of altered reflexes were detectable even when normotensive obese adults (defined in studies as systolic/diastolic blood pressure <140/90 mmHg) were tested [62], suggesting that early detection of these abnormalities can be used as a prognostic tool. Weight loss induced by a hypocaloric diet partially reversed the attenuated metaboreflex response [75] and improved baroreceptor sensitivity in obese normotensive individuals [63]. In addition, weight reduction induced favorable adaptations on the MSNA responses during mental stress in obese women and improved forearm vascular conductance at rest [76]; however, these beneficial adaptations were only obtained when the hypocaloric diet (600 kcal/day dietary reduction) was accompanied by exercise training and not by a similar dietary caloric restriction alone [76]. The diet plus exercise training group in that study performed three 60 min exercise sessions per week of aerobic (40 min per session) and strengthening exercise for four months. Since both groups exhibited a similar weight loss and changes in body composition were not assessed, it is not clear whether increases in lean body mass and a greater decrease in percent body fat resulted in the beneficial effects on MSNA and vascular conductance. Moreover, the effects of weight loss and weight loss maintenance on sympathetic activity might be divergent and organ-specific adaptations might exist. Straznicky et al. [77] showed that after weight maintenance, the beneficial effects of weight loss on norepinephrine spillover rate were preserved, whereas MSNA and baroreflex sensitivity

adaptations were not maintained. Future studies should examine the mechanisms by which exercise training exerts advantageous alterations in the exercise pressor reflex and investigate whether the beneficial effects on sympathovagal control are linked to changes in body composition. The effects of resistance training or high intensity exercise, as well as possible gender differences in the exercise pressor reflex and the muscle metaboreflex should also be investigated.

6. Control of Blood Pressure at Rest and during Exercise in Obese Children

The autonomic nervous system undergoes changes from childhood to adulthood. Body size, muscle characteristics, energy systems involved, and arterial stiffness also change [78–80]. Therefore, applying the information that we have learned from studies in obese adults to studies in obese children, might be not be appropriate. Up-to-date, only a few studies have directly compared the blood pressure responses and the sympathovagal involvement to the control of the exercise pressor reflex in children and in adults. A lower response of blood pressure (using finger photoplethysmography) during isometric handgrip exercise and lower baroreceptor sensitivity has been reported in children than in adults [81]. However, the exercise pressor reflex in that study was examined as a whole, involving all peripheral reflexes; therefore the role of the each of the reflexes (metaboreflex, mechanoreflex) to the control of blood pressure in children is not clear. Only one study [82] attempted to isolate the exercise-induced increase in metabolite concentration (using circulatory occlusion) to the control of blood pressure during handgrip exercise in children and reported similar responses in children and in adults. In the latter study, the blood pressure measurements were not performed on a beat-by-beat basis and the sympathetic/vagal involvement to the blood pressure response was not examined. Furthermore, faster postexercise hemodynamics have been reported in young children compared with adolescents [83] and adults [84, 85], linked with a faster parasympathetic outflow [81] or changes in lean body mass and blood acidosis [83, 86].

In children, increased levels of adiposity have been partially linked to autonomic nervous system dysfunction and an increased prevalence of hypertension in adulthood [87]. Yet, the exact mechanisms by which childhood obesity leads to hypertension remain unclear. Increased resting blood pressure [88], reduced baroreceptor sensitivity [89], and decreased resting forearm blood flow have been reported from an early stage in obese children [90]. During sympathetic stimulation induced by isometric handgrip exercise, the arterial blood pressure response has been reported similar [15] or higher [88] in obese compared with lean aged-matched children. Differences in reported blood pressure responses could be partly or collectively explained by (i) basal blood pressure differences, (ii) variations in body fat distribution [91], (iii) differences in participants' age, since cardiovagal autonomic function undergoes a gradual maturation during childhood [92], and (iv) method of blood pressure measurement (continuous beat-by-beat finger photoplethysmography, or intermittently every 60 or 120 s by a conventional aneroid sphygmomanometer). Genetic factors and family history of hypertension can also be contributing factors, since offsprings of parents with a family history of hypertension exhibit higher basal blood pressure levels and greater mean arterial pressure during mental stress and handgrip exercise than children of normotensive parents [93]. Low fitness levels can also exaggerate the blood pressure response to exercise in children with obesity. In a recent study by Legantis et al. [94], obese and overweight unfit children exhibited an exaggerated systolic blood pressure response (assessed by finger photoplethysmography) during isometric handgrip exercise compared with their fit overweight and obese counterparts.

Even in the absence of any alterations in resting blood pressure, signs of disturbed hemodynamic control during acute isometric handgrip exercise (at 30% MVC) and recovery were evident in obese prepubertal boys [15]. Dipla et al. [15] reported an attenuated increase in exercise heart rate, associated, at least partially with a lower vagal withdrawal in obese compared with lean boys. However, the magnitude of the blood pressure response to exercise (assessed as the change from baseline, using beat-by-beat finger photoplethysmography) was similar in lean and obese boys. In addition, a lower decline in baroreceptor sensitivity during isometric exercise was found in obese versus lean preadolescent children [15].

During dynamic exercise, a blunted muscle perfusion response to lower limbs has been reported in overweight children [66], possibly linked with arterial endothelial dysfunction [56, 95]. Furthermore, early signs of vascular dysfunction in obese children have been demonstrated in the postexercise period, as evident by a reduced capacity for vasodilatation in the recovery from isometric exercise in obese compared with lean boys [15]. These vascular reactivity dysfunctions during exercise (dynamic or isometric) and recovery, are possibly also the result of accumulation of perivascular adipose tissue (surrounding the blood vessels) and intima media thickening [96].

Isolating the metaboreflex activation by postexercise occlusion, Dipla et al. [15] found similar blood pressure responses in normotensive obese and lean prepubertal children. However, the relative contribution of total peripheral resistance and stroke volume to this response was altered in obese preadolescent boys, even in the absence of a fully developed metabolic syndrome.

A limitation of studies currently available in children is that the autonomic nervous system involvement during exercise was assessed indirectly, using hemodynamic parameters and not direct measurement of norepinephrine spillover rate or MSNA. Although heart rate variability provides an indication of the heart's ability to respond to multiple physiological stimuli and can identify phenomena related to autonomic nervous system, it is not considered as precise as the measurement of norepinephrine spillover. However, its noninvasive and nonpharmacologic nature makes it appealing for use in the pediatric population, especially when healthy lean children participate as controls.

7. Effects of Training and Physical Activity on Blood Pressure Control

This section will first discuss findings in studies examining the effects of training to the neural control of blood pressure in obese adults and then continue with findings in obese children. In a large cohort study, Felber-Dietrich et al. [97] showed that participation in regular physical activity programs has beneficial effects on cardiac autonomic function (assessed by 24-hour recordings of heart rate variability) and tends to offset the negative effects of obesity on autonomic nervous system indices. More specifically, obese individuals exercising regularly >2 h/week exhibited heart rate variability values closer to those obtained by normal weight individuals. Cardiac autonomic function in those who gained weight while exercising regularly was improved compared to sedentary subjects who gained weight. Although a major strength of that study is the involvement of a large number of participants, a limitation is that the amount of physical activity was assessed by a questionnaire. In addition, since body composition was not assessed in that study, it is possible that the observed improvements in autonomic function in the active obese individuals, is at least partly the result of an increase in their lean body mass. The important role of physical activity on vascular health has been demonstrated by a study showing that cessation of physical activity in healthy adults during bed rest resulted in a rapid decline of vascular reactivity (within 3–5 days) [98]. Aerobic exercise training in obese individuals induces metabolic alterations, such as increases in bioavailability of nitric oxide and in glucose transporter (GLUT-4) concentration within the skeletal muscle and increases in the number of highly oxidative and insulin-sensitive type I fibers in adults [99, 100]. These changes have been associated with improved endothelial cell function (assessed by brachial artery flow mediated dilatation) [99]. Whether improvements in the autonomic nervous system function in response to training contribute to these alterations remains to be elucidated.

Early detection of vascular dysfunction is important to initiate behavioral interventions to reduce the risk of developing cardiovascular disease. In children, sedentary behavior is a major factor linking adiposity to insulin resistance, inflammation, and endothelial dysfunction. Controlled studies that examine whether exercise training interventions reverse the alterations observed in baroreflex sensitivity and in the exercise pressor reflex in obese children are not currently available. Previous studies have indicated that exercise training improves vascular reactivity. More specifically, Watts et al. [101] showed that obese children and adolescents had a 50% lower vascular reactivity compared with their control peers during rest and reduced free-living physical activity was related to vascular dysfunction (assessed by flow-mediated dilatation) in children [102]. Furthermore, Hopkins et al. [103] showed that the amount of moderate to vigorous activity was closely associated with increased vascular reactivity and health. Prado et al. [104] showed that a hypocaloric diet accompanied by exercise training, accelerated the postexercise heart rate recovery, more than diet alone, suggesting an additive effect of increased cardiorespiratory fitness by exercise training on cardiac autonomic activity. Importantly, the improved arterial endothelial function following an eight-week aerobic exercise training program was evident even in the absence of weight reduction in overweight children [99]. These results highlight the importance of increased fitness levels in vascular health in obese and overweight children [94] and imply that metabolic and hormonal adaptations induced by exercise training plays a major role in lowering risk factors.

In many studies that examined the effect of weight loss on the reflexes involved in the blood pressure control and the involvement of exercise training, it was difficult to isolate the effect of physical activity, independent of changes in body mass consequent to the intervention. In addition, differences in the definition of overweight/obesity among studies, especially in the pediatric population (based on body mass index $\geq 30\,kg/m^2$ versus body mass index > 95th percentile for age and gender) [105], as well as differences in the assessment of childhood or adolescence (based on age versus maturation status using Tanner stage or age at peak height velocity—i.e., the time of maximum growth in stature during adolescence) have created controversies among studies.

8. Overall Summary and Recommendations for Future Research

Given the above findings, a hyperadrenergic state is a hallmark of obesity; however, a differentiation of central nervous system sympathetic outflow, with increased traffic in the renal and skeletal muscle sympathetic nerves and reduced cardiac sympathetic nerve firing is evident in obese individuals. These alterations lead to adjustments in the reflexes that control blood pressure. We can conclude that even when not accompanied by an elevation in arterial blood pressure, alterations in the sympathovagal involvement (at rest and during exercise) may be evident in an obese individual. Adaptations in reflexes including a blunted baroreflex sensitivity, lower metaboreflex, and possibly a greater involvement of mechanoreflex appear even in the preadolescent years. These changes, accompanied by the endothelial dysfunction, result in alterations in hemodynamic control (such as differences in the heart rate responses and vasodilatation) during exercise and recovery. Despite considerable achievements in our understanding in the control of blood pressure in obesity, several issues remain unclear. What cellular and molecular events mediate the alterations in the reflexes that control blood pressure during exercise in obesity? Additional experimentation is required to address the possible mechanisms that reverse these pathological events. Another area of implementation should be the assessment of different exercise training modes (continuous or intermittent, dynamic or isometric) and exercise intensities (high versus low) required to induce beneficial regressions in the reflexes controlling blood pressure in obesity. Importantly, studies involving training interventions should be designed to specifically stratify the independent effect of exercise versus dietary modification. To date, the efficacy of antiadrenergic, antihypertensive drugs to the regression of the alterations observed in the exercise pressor reflex has not been tested.

Future studies should also explore the role of alterations in the macronutrient intake percentages to the blood pressure responses during exercise in obese adults, as well as in the pediatric population.

Conflict of Interests

The authors claim no conflict of interest in the submitted paper.

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