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EDITORIAL

"Broken" autonomic cardiac circadian clock in obese adolescents: evidence and implications

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In the present issue of *Clinical Autonomic Research*, Rodriguez-Colon et al. [1] examine the behavior of 24-h heart rate profile in a large cohort of adolescents recruited in the follow-up of the Penn State Children Cohort Study. Specifically, the authors performed power spectral analysis of the 24-h heart rate signal in order to determine whether and to what extent the high-frequency/low-frequency components of the R–R interval, which are well known to represent reliable indices of parasympathetic/sympathetic cardiac drive, respectively [2], are altered in these subjects. Data that were analyzed by adjustments for confounders (specifically age and gender) were compared to those obtained in non-obese children and adolescents. The results expand previous information collected on this topic [3–6], by showing that the circadian pattern of parasympathetic and sympathetic control of the heart rate signal is altered in these young groups of obese. They also provide evidence that the alterations in vagal modulation of sinus node activity are manifest in both genders, independently of the subject's age and over the whole 24-h period. However, when circadian curves of estimated high-frequency components detected in obese and control subjects are compared, it becomes clear that the difference in the two curves is greater for magnitude in the daytime period between 6.00 a.m. and 2.00 p.m. This time window includes the early morning hours known to be associated with a pronounced adrenergic overdrive to the heart and peripheral vessels, and with a greater risk of sudden arrhythmic death, particularly in obese patients [2, 7].

Although technically well performed and founded on a solid database, the study by Rodriguez-Colon et al. [1] has a number of limitations. First, unfortunately, no data are available on the relationships between the high-frequency/low-frequency heart rate patterns and waist-to-hip ratio, which is a sensitive marker of body fat distribution [7]. This information is needed to determine whether the observed cardiac autonomic dysregulation was more pronounced in people with visceral fat obesity, or people with peripheral fat obesity, as it has been reported in obese adults [8, 9]. More importantly, these missing data would have given the researchers an opportunity to more closely link the autonomic dysfunction to the metabolic alteration, which is a hallmark of the central type of body fat depot, i.e., insulin resistance [7, 8]. The second limitation refers to the fact that the neural alterations reported in the present study strictly refer to cardiac autonomic drive and not to the overall cardiovascular autonomic function. In other words, the data collected by Rodriguez-Colon et al. [1] do not provide any insight on the behavior of sympathetic neural function in cardiovascular districts other than the heart. This is because no relationship exists between the data collected by the power spectral analysis and those obtained via direct measures of sympathetic drive, such as those collected via the microneurographic recording of efferent postganglionic muscle sympathetic nerve traffic in the peroneal nerve [10]. Finally, in the study by Rodriguez-Colon et al. [1], information is available on the presence, as well as the severity, of the sleep apnea syndrome in the obese adolescents studied, and thus, on the independent effects, this obesity-related complication may have on parasympathetic and sympathetic neural function [2, 11, 12].

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The intriguing results of the study by Rodriguez-Colon et al. [1] offer the chance to briefly address in the second part of this editorial two relevant practical questions, i.e., (1) why we should care about the study findings and (2) whether the described circadian autonomic abnormalities are irreversible, or if they can be favorably affected by a given therapeutic intervention.

As far as the first question is concerned, it should be noted that the loss of autonomic balance in terms of a reduced parasympathetic (protective) tone with a parallel augmentation of the sympathetic excitatory (detrimental) influences is responsible for well-recognized adverse effects in obese individuals independent of the patient's age. These include an increase in peripheral vascular resistance, which in conjunction with the sodium retention by the kidney and the renin-angiotensin stimulation (both processes being triggered by the adrenergic activation [2]) may favor the development and progression of a blood pressure increase [13]. These also include the metabolic abnormalities, with a particular emphasis on the development and progression of an insulin resistance state which again has a promoting role in the genesis of the sympathetic overdrive [2, 8, 9, 14]. They finally include the development of heart failure and life-threatening cardiac arrhythmias, given again the relevance of the sympathetic overdrive in the pathophysiology of these two frequent cardiovascular complications of the obese state [2, 15, 16].

Is the altered autonomic circadian profile reversible by adequate therapeutic interventions? Studies in adult obese patients clearly show that this is the case. Indeed, regular physical exercise has been clearly shown to improve autonomic balance by exerting an inhibition of the sympathetic excitatory effects and, throughout a baroreflex potentiation, a clear-cut reinforcement of vagal cardiac drive [2, 17]. Similar results can be achieved by introducing a hypocaloric diet, which may reduce body weight by at least 10 % [18]. Recently, an improvement in autonomic cardiovascular drive has been described in middle-aged severly obese patients who have had the sleeve gastrectomy procedure, which resulted in a consistent and stable reduction in body weight [19, 20]. The autonomic effects of all the abovementioned procedures, however, have been so far investigated mainly in obese adult individuals with different levels of clinical severity. Whether these procedures may be applicable and effective also in young and adolescent obese individuals remains to be seen.

Conflict of interest None.

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