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CLINICAL FEATURE
REVIEW

Asymptomatic bradycardia amongst endurance athletes

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ABSTRACT

It is established that an intensive training results in a lower average resting heart rate. Management of bradycardia in an athlete can be difficult given the underlying mechanisms are not clearly understood. The authors reviewed the different mechanisms described in the literature, including recent advances in physiology regarding remodeling of ion channels, which may partially explain bradycardia in athletes. Sinus bradycardia amongst athletes, especially endurance focused athletes, is common but difficult to apprehend. The underlying mechanisms are observably of multifactorial origin and likely incompletely elucidated by the current body of knowledge.

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Background

Extreme training of high endurance athletes such as cyclists, triathletes, and marathon runners has been documented to have notable consequences on heart rhythmic function. Compared to the general population, people who practice extreme training have a greater occurrence of sinus bradycardia (Figure 1) [1]. Bradycardia is usually defined as a resting frequency below 60 beats per minute (bpm). In athletes, data suggest a lower threshold of 50 bpm (Figure 2) [2,3]. Sinus bradycardia is found in 50–85% of athletes in all disciplines, and in more than 90% of enduring athletes [4–6]. These athletes are often asymptomatic and the diagnosis is a fortuitous discovery [7]. Severe bradycardias with a heart rate under 40 bpm are found in approximately 4% of athletes in all disciplines [4,8]. Clinical cases report extreme bradycardias with a heart rate under 30 bpm, mostly in endurance sports [9–11].

Management of asymptomatic bradycardia in an athlete can be difficult given the underlying mechanisms are not clearly understood. Recent advances in bradycardia etiology have revived the multifactorial origin debate.

Physiology of heart rate regulation

To better understand the mechanisms responsible for bradycardia, it is imperative to revisit the physiology of heart rate regulation. Three key factors drive heart rate regulation: the pacemaker cells of the sinus node, the parasympathetic nervous system, and the orthosympathetic nervous system.

Pacemaker cells are located on the superior portion of the right atrial wall at the sinoatrial node. Cyclical local depolarization results in the generation of action potentials resulting in automatism of surrounding myocardiocytes [12]. In humans, the intrinsic frequency of this process is approximately comprised between 100 and 120 bpm. The action potentials of pacemaker cells differ from those of contractile myocardial cells by the presence, in phase 4, of a spontaneous diastolic depolarization slope which is the key factor for generation of cardiac rhythm (Figure 3).

Several channels play a prominent role in the generation of the diastolic depolarization such as the L-type voltage-gated calcium channels or hyperpolarization-activated cyclic nucleotide-gated (HCN) channels, also known as funny channels (permeable to sodium and potassium) [13–16].

These funny channels are a major player in both generation of spontaneous activity and rate control dependent on the autonomic, parasympathetic and orthosympathetic nervous system [17].

The parasympathetic nervous system is integrated at the cardiac level by the vagus nerve. The binding of acetylcholine with muscarinic receptors causes the down-regulation of intracellular cyclic adenosine monophosphate (cAMP) resulting in decreased funny channel recruitment [18]. As funny channel recruitment decreases, diastolic depolarization time increases and, subsequently, heart rate decreases.

The orthosympathetic nervous system is constitutively active in order to maintain homeostasis. Secretion of catecholamine stimulates a decrease in the diastolic depolarization time, resulting in an acceleration of the heart rate. The relationship between depolarization time and heart rate of the orthosympathetic system are therefore in juxtaposition to the relationships observed with the parasympathetic nervous system [1,3,5,9,19].

Pathophysiology of bradycardia in athletes

Several mechanisms have been studied to understand the physiological factors underlying athletic conditioning induced bradycardia. Previously, the autonomic nervous system was

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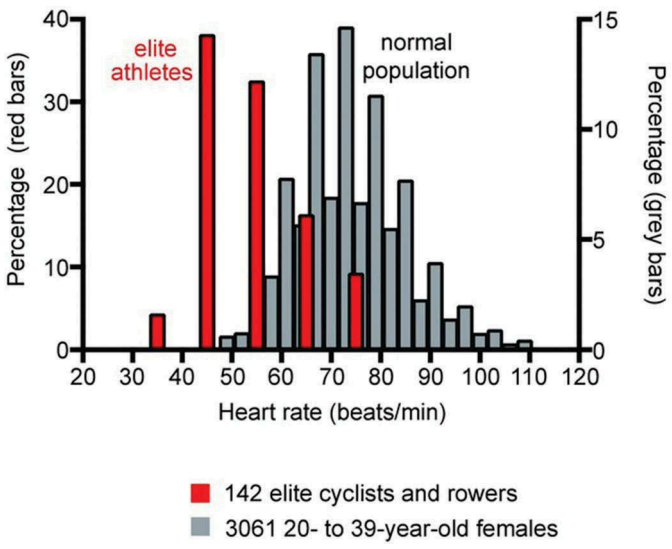

Figure 1. Resting heart rates in elite athlete versus the normal population. Reproduced from D'Souza et al. [3], with permission. © 2015 The Authors. The Journal of Physiology published by John Wiley & Sons Ltd on behalf of The Physiological Society.

considered the main modulator [19]. The vagal hypertonia has also extensively been investigated as a causative mechanism, although technology has not yet been able to record the activity of the vagus nerve on a human heart due to the presence of efferent and afferent fibers. However, when the vagus nerve activity is blocked with a pharmacological agent (atropine), we observe a lower heart rate in trained patients compared to those who are sedentary [20].

Autonomic balance then becomes a topic of interest, specifically in determining whether the emphasis on vagal tone is independent from decreased orthosympathetic tone [21,22]. Observing purely orthosympathetic activity of the peroneal nerve, the number of electric discharges following the Valsalva maneuver is decreased in a trained subject compared to a non-trained subject [22]. Therefore, it could be speculated that orthosympathetic hypotonia may result in an overexpression of the parasympathetic tone without simultaneously observing vagal hypertonia.

Bradycardias are secondary to intensive workouts that induce cardiac remodeling. The purpose of cardiac remodeling is to promote better stroke volume during exercise, ensuring a higher cardiac output. A higher stroke volume generates an increase in blood pressure relative to the volume of an equivalent normal heart rate [23]. As the body adapts, through the action of baroreceptors, regulation of the sinus node reduces cardiac output. This may explain the underlying mechanism seen in athlete's heart [24].

Athlete's heart is more commonly seen in enduring athletes who train more than 6 h per week at more than 60% of the maximal oxygen consumption. It is characterized by a harmonic enlargement of cardiac cavities with wall hypertrophy [5,24].

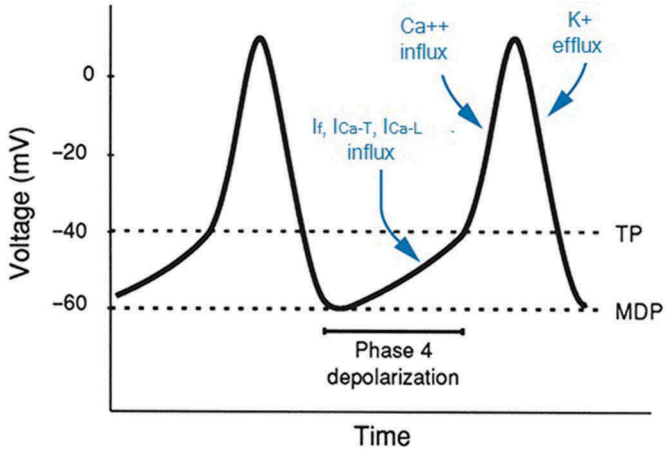

Figure 3. The action potentials of a pacemaker with, in phase 4, a spontaneous diastolic depolarization slope. MDP, maximum negative diastolic potential. TP, threshold potential.

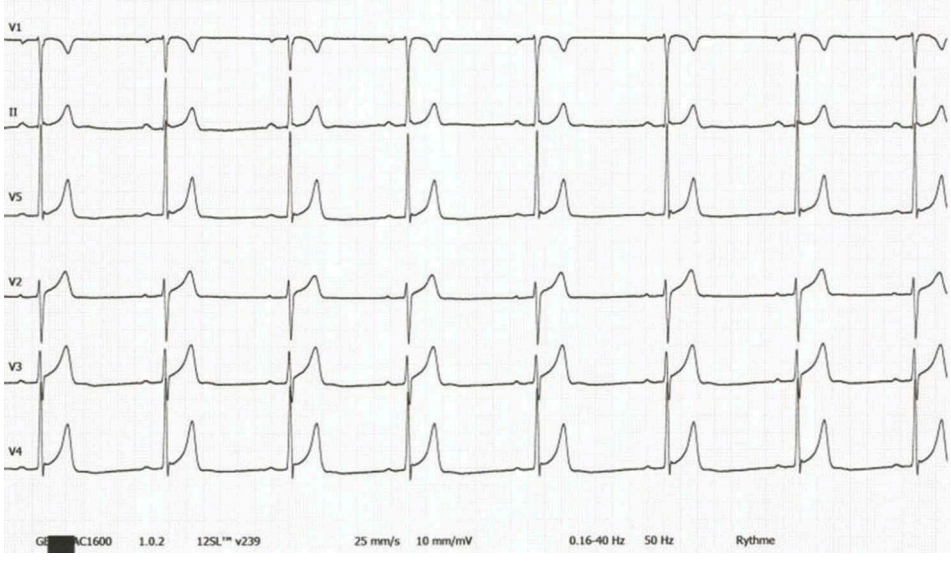

Figure 2. Electrocardiogram showing sinus bradycardia (38 bpm) obtained from a professional cyclist.

Recent data have driven the field into new ideologies. Despite complete pharmacological blocking of the para and orthosympathetic nervous systems (atropine and beta blockers), a lower heart rate persists in athletic subjects when compared to controls [20]. On the other hand, when observing denervated cells, correlations between heart rate and spontaneous variability of the R-R interval persist [25]. These data suggest the possibility of modifications within the sinus node itself. In 2006, a study observed a family of bradycardic patients and identified a mutation in the gene coding for HCN4 proteins. It is located near the cAMP binding site [26]. This is the site where the cAMP binds to activate the channel. Mutated channels typically responded to cyclic AMP with a greater negative voltage than non-mutated channels resulting in an increased diastolic depolarization time, similar to the parasympathetic mechanism of regulation, resulting in a bradycardic effect.

D'Souza's team in England investigated HCN4 channel proteins with a focus on under-expression and the resulting decrease in funny channel frequency between trained and normal mice [1]. Since the number of funny channels decreased among trained mice, the depolarization slope was lower during hyperpolarization, resulting in slowing of the intrinsic heart rate. These data are further validated through the observation of positive pharmacological blocking of funny channels causing a normalization of the heart rate across both groups of mice [27,28].

Other studies on the mice and rats previously demonstrated that the expression of HCN4 channel proteins may become variable during pregnancy, in animals with metabolic syndromes, or animals with pulmonary arterial hypertension [29,30]. Beyond the remodeling of ion channels secondary to intensive training, it is clear that a genetic component is also present and plays a role in the intrinsic frequency of the sinus node among individuals of the same family.

Clinical presentation

Endurance athletes are more likely to develop sinus bradycardia and myocardial remodeling is observed during echocardiography in these athletes. Most bradycardias are between 40 and 50 bpm, with lower frequencies rarely observed. It is interesting to note that amongst these athletes, there is no correlation between the severity of bradycardia and the PR interval, further validating the arguments against a purely parasympathetic pathophysiology [5].

Asymptomatic sinus bradycardia is frequently found in high-level athletes. However, a heart rate below 35 bpm is rare, appearing only in extreme endurance athletes. Sinus arrhythmias occur in conjunction with the presentation of bradycardia. It is possible to find junctional rhythms, wandering pacemaker, sinus pauses, atrioventricular conduction delays (first and second degree Mobitz 1) as well as isorhythmic atrioventricular dissociation among 70% of bradycardic athletes [2–7]. These benign arrhythmias are more frequently observed while sleeping, due to parasympathetic predominance.

When utilizing established electrocardiographic interpretive criteria, individuals classified as normal athletes demonstrate bradycardia [31]. The degree of variability found across athletes therefore requires no further investigation [32]. The European Society of Cardiology recommends an asymptomatic patient with a resting heart rate above the lower limit of 30 bpm may be considered normal for the top athlete, and requires no further examination [33]. Presence of bradycardia alone does not merit treatment.

However, in the presence of suggestive symptomatology, it is clear that any bradycardia must be investigated by performing a stress test, a Holter monitor, or an electrophysiological study when a Hisian or infra-Hisian block is suspected. Pause times greater than 2 s during waking hours, the absence of return to sinus rhythm during a stress test, or third-degree atrioventricular block must also be subjected to further examination.

Conclusion

Sinus bradycardia amongst athletes, especially endurance focused athletes, is common. The underlying mechanisms are observably of multifactorial origin and likely incompletely elucidated by the current body of knowledge. Nevertheless, in the absence of symptoms, sinus bradycardia with a heart rate greater than 30 bpm in a high-level athlete does not require further investigation or treatment.

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Declaration of interest

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