Physiological rate adaptation in a child with chronotropic incompetence through closed-loop stimulation using epicardial leads

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Introduction

Chronotropic incompetence may lead to increased myocardial stress during mental loads, as the circulatory demand has to be provided with an increase in myocardial contractility because of insufficient heart rate increases.[1]

Closed-loop stimulation (CLS) is a form of rate-adaptive pacing designed to mimic the physiologic response of a normal sinus node, by monitoring changes in ventricular contractility and adapting the pacing rate accordingly. This type of closed-loop rate adaptation is sensible to non-exercise-related demands as well, such as postural, mental, and emotional stress.[2]

CLS modulates heart rate on the basis of an indirect measurement of ventricular contractility, which increases during catecholamine stimulation, as occurs during exercise and emotional stresses. The ventricular contractility is estimated from the measurements of the electrical impedance of the cardiac tissue in close proximity to the catheter tip. To estimate the electrical impedance, the device delivers subthreshold unipolar pulse trains in a 350 ms window following each paced or sensed ventricular depolarization. The ventricular contractility is estimated from the slope of the electrical impedance increases during systole: the higher the slope, the higher the contractility.

CLS adaptation to an individual patient's contractility is fully automated and, in most cases, advanced parameter programming is not required.

The main advantage of the CLS compared to other conventional algorithms that modulate heart rates, such as those using accelerometers and/or minute ventilation measurements, is its unique ability to adapt heart rate on a beat-to-beat basis, even in response to nonphysical stresses, by quickly responding to changes in sympathetic activity. This is done through the continuous monitoring of the inotropic state of the heart, which is not performed by either accelerometer-based or minute ventilation-based algorithms.

CLS is normally used with endocardial right ventricular leads. However, it has been shown that CLS might also be capable of heart rate modulation in pediatric patients when connected to an epicardial lead.[3] Nevertheless, a full assessment with nonphysical stresses has never been attempted. In this report we present for the first time the analysis of CLS rate response to both physical and mental stresses in a child with a postsurgical chronotropic incompetence and a dual-chamber epicardial pacing system.

Case report

An 8-year-old child was referred for pacemaker (PM) implantation for postsurgical sinus node dysfunction. Her clinical history was characterized by a prenatal diagnosis of partial atrioventricular (AV) septal defect with normal karyotype. She underwent primary repair followed by 5 surgical procedures because of a left AV valve dysfunction and subaortic stenosis: 1) mitral surgical valvuloplasty; 2) mitral valve replacement with Kabbani technique; 3) mitral valve replacement with mechanical prosthesis n.16; 4) subaortic membrane resection; and 5) a new subaortic membrane resection. In the last surgery, 2 unipolar atrial and ventricular epicardial leads (Medtronic Capsure Epi 60 cm) were placed, respectively, on the right appendage and the diaphragmatic surface of the right ventricle and tunneled inside a left paraumbilical abdominal pocket. During the follow-up she reported fatigue and exercise intolerance with episodes of dizziness at rest or soon after physical activities. The baseline electrocardiogram (ECG) showed sinus

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KEY TEACHING POINTS

- Closed-loop stimulation (CLS) has provided long-term heart rate modulation on a wider frequency range as compared to the projected accelerometer profile, even in combination with an epicardial lead.

- The experimental stress test model used in this case report appears suitable to evaluate the efficacy of CLS pacing mode with epicardial leads in pediatric patients.

- The results of this case report may open the way to safe and efficient tests for CLS with epicardial leads, although there is little chance of a prospective study owing to the limited number of patients.

bradycardia at 55 beats per minute (bpm) rate with normal AV conduction. Echo examination revealed a normally functioning mitral prosthesis and a low subaortic residual peak gradient of 20 mm Hg. She then underwent a 24-hour Holter monitoring that showed normal AV conduction and sinus bradycardia (mean heart rate of 72 bpm) with short (less than 2 seconds) sinus pauses followed by periods of escape narrow QRS junctional rhythm. A treadmill stress test to exhaustion definitively highlighted choronotropic incompetence with a baseline heart rate of 62 bpm and a maximum heart rate at peak exercise of 140 bpm. Therefore, an indication for rate-adaptive permanent pacing was given owing to symptomatic sinus node dysfunction. A dual-chamber pacemaker (EVIA DR [-T]; Biotronik, Berlin, Germany) was connected to the previously implanted epicardial leads and positioned in an abdominal pocket. The symptoms improved after implantation of the pacemaker. After CLS activation, rate adaptation was evaluated through the analysis of the data stored in the device memory for long-term assessment and with a specific test session consisting of a physical and 2 mental tasks, selected on the basis of the patient's age and education: sustained isometric handgrip exercise, video game (Subway Surfers) playing, and Stroop color-word test (CWT). The CWT is often used as a standardized test to evoke experimental stress when researching cardiovascular functions.[4] Informed consent was obtained from the patient's parents. During each session, surface ECG was continuously acquired and stored thanks to a digital ECG recording system (Cardioline, Trento, Italy). Instantaneous heart rate was extracted off-line by using a previously validated R-wave detection algorithm.[2] All the detected beats were then visually inspected to remove/correct misdetections/misclassifications.

At the time of the test, the PM programmed parameters were as follows: lower rate 65 bpm, maximum CLS pacing
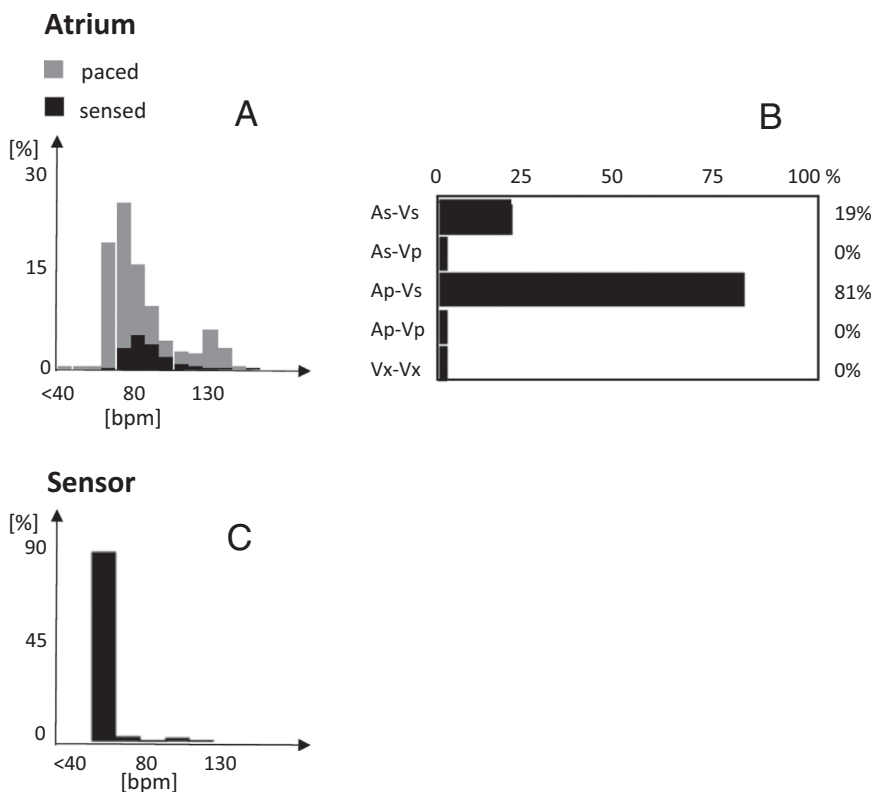
Figure 1 Diagnostic data extracted from the device since the last follow-up (133 days). **A:** Histogram of the atrial paced and sensed beats, represented as gray and black bars, respectively. The histogram shows the percentage of paced and sensed beats as a function of their own heart rate. **B:** Representation of the percentage number of atrial-ventricular sequences; As = atrium sensed; Ap = atrium paced; Vs = ventricle sensed; Vp = ventricle paced. **C:** Histogram of the sensor activity. The histogram shows the percentage number of beats as a function of the heart rate that the accelerometer would impose, if activated.

rate during physical activity 155 bpm, without physical activity 85 bpm, AV delay 250 ms (AV hysteresis 400 ms).

Figure 1 shows the 4-month rate distribution of paced and sensed atrial beats (Figure 1A) and the percentages of AV sequences (Figure 1B). More than 80% of atrial beats were paced events, further confirming the chronotropic incompetence. Figure 1C shows the projected heart rate profile that would have been obtained if the accelerometer sensor had been used for rate responsiveness instead of CLS. This special function of the used device allowed direct comparison between CLS (Figure 1A) and accelerometric sensor (Figure 1C) rate profiles within the same follow-up interval: the CLS algorithm modulated the pacing rate in a wider frequency range (resembling normal heart rate profiles), in response to different detected stresses. On the other hand, the accelerometer sensor would have generated more than 90% of paced beats below 80 bpm.

Figure 2 shows the heart rate trends in basal condition and during the 3 stress tests. At rest the percentage of pacing was close to 100%. Spontaneous rhythm emerged at the very beginning of the handgrip and disappeared as soon as the muscle effort terminated; then a paced rhythm took over, gradually decreasing the heart rate to the pretest value. During the video game playing the CLS-paced heart rate increased up to 85 bpm; no spontaneous beats were observed. During CWT the heart rate showed a variable pattern, characterized by a continuous mix of spontaneous and paced beats, at very similar instantaneous heart rates.

Discussion

CLS is a pacing algorithm that modulates the pacing rate according to an indirect measurement of the ventricular contractility. As ventricular contractility is modulated by the autonomic nervous system, the CLS algorithm should provide a physiological rate adaptation as compared to other sensors. Technically, the assessment of ventricular contractility is obtained by a measure of the electrical impedance of the heart tissues surrounding the tip of an endocardial lead. The cardiac tissue area involved in this measurement is about 1 cm around the lead tip (Figure 3). Given the thickness of the cardiac wall in pediatric age, CLS could work even with an epicardial lead. In pediatric patients, modulation of heart rate not only during exercise but also during emotional stress and cognitive tasks is pivotal. In this case report, the histogram of the atrial paced beats has provided evidence of the ability of CLS to modulate heart rate during daily life.

Even with the epicardial lead, the CLS algorithm modulated the heart rate over a range of frequencies (70-150 bpm, Figure 1A) remarkably wider than what an accelerometric sensor would have done (Figure 1C).
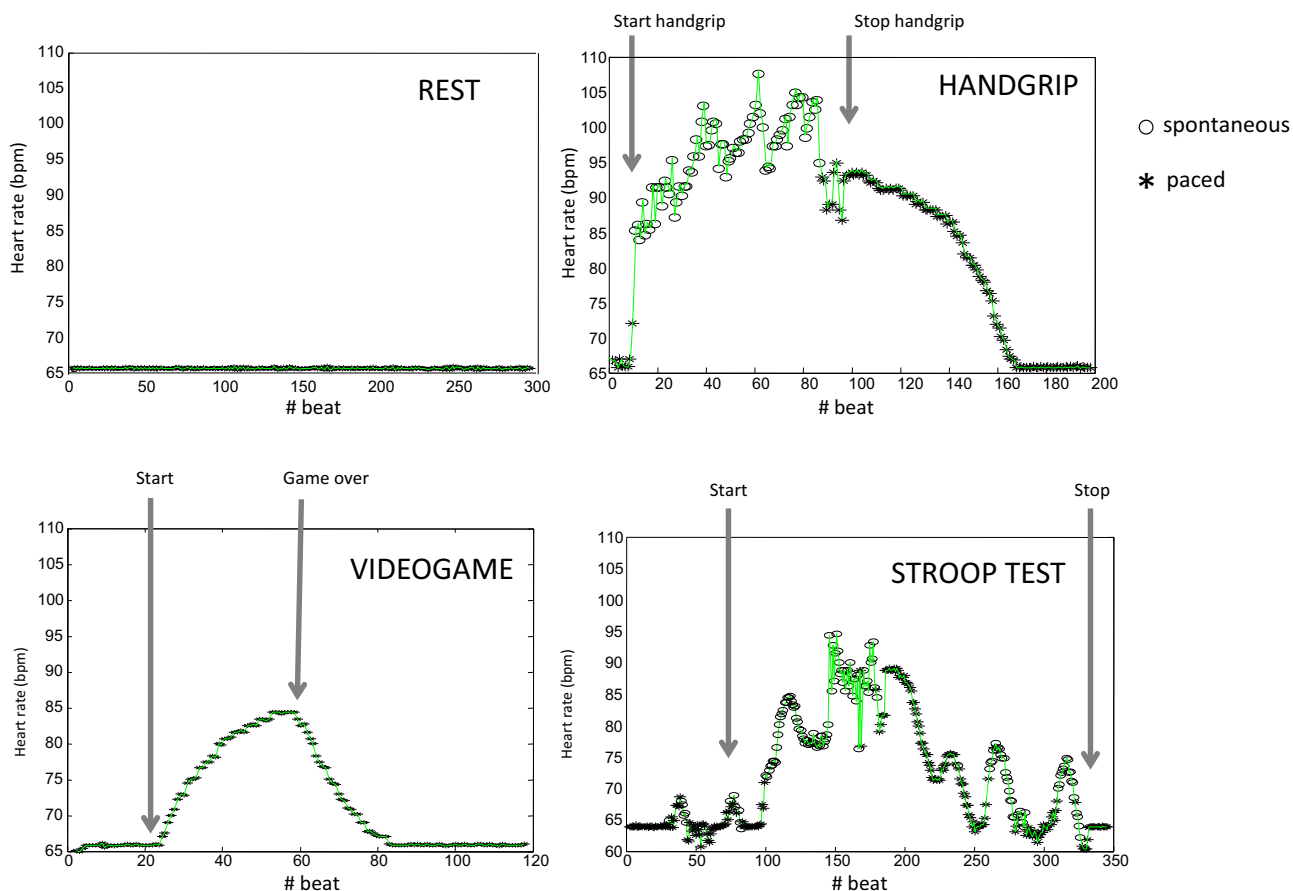
Figure 2   Heart rate during the 4 test sessions: basal heart rate, handgrip, video game playing, and Stroop color-word test. Heart rate (as beats per minute [bpm]) is reported as a function of the number of beats (# beat). Circles indicate the spontaneous beats; stars indicate the paced beats.

Figure 3   Cardiac area involved in closed-loop stimulation impedance measurements.

The neurovegetative tests demonstrated the physiological behavior of the CLS algorithm in response to both physical and mental tasks. Indeed, as already observed using endocardial leads,[2,3,5,6] the CLS behaves differently accordingly to the nature of the stress: the maximum heart rate value reached during handgrip is higher than that reached during the mental tests (video game playing and Stroop test).

The autonomic effector mechanisms in response to the given stressors (ie, withdrawal of the vagal tone vs increase of sympathetic influence) have different weight and timing, and this can explain the different pattern of spontaneous and paced beats observed. During the handgrip, vagal withdrawal provides the early response, while sympathetic effects appear later.[7] This mechanism might explain the abrupt emergence of a spontaneous rhythm as soon as the muscle effort starts. During mental tasks, the autonomic effectors act together with a resulting random pattern of spontaneous and paced beats, which mix harmonically without abrupt changes of the instantaneous heart rate.

In conclusion, the CLS has provided long-term heart rate modulation on a wider frequency range as compared to the projected accelerometer profile, even in combination with an epicardial lead. The experimental stress test model used in this case report appears suitable to evaluate the efficacy of CLS pacing mode with epicardial leads in pediatric patients. The results of this case report may help in planning safe and efficient tests for CLS with epicardial leads, although there is little chance of a prospective study owing to the limited number of patients. Although the benefits deriving from physiological heart rate modulation in pediatric patients with pacing indication are potentially remarkable, collecting different experiences in a multicenter registry might be a practical option.

Acknowledgments

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