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Review

The influence of age and weight status on cardiac autonomic control in healthy children: A review

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ABSTRACT

Heart rate variability (HRV) analyses can provide a non-invasive evaluation of cardiac autonomic activity. How autonomic control normally develops in childhood and how this is affected by obesity remain incompletely understood. In this review we examine the evidence that childhood age and weight status influence autonomic control of the heart as assessed using HRV. Electronic databases (Pubmed, EMBASE and Cochrane Library) were searched for studies examining HRV in healthy children from birth to 18 years who adhered to the Task Force (1996) guidelines. Twenty-four studies met our inclusion criteria. Seven examined childhood age and HRV. A reduction in 24-hour LF:HF was reported from birth to infancy (1 year), while overall HRV (SDNN) showed a marked and progressive increase. From infancy to early-to-late childhood (from 12 months to 15 years) LF:HF ratio was reported to decline further albeit at a slower rate, while RMSSD and SDNN increased. Twenty studies examined the effects of weight status and body composition on HRV. In a majority of studies, obese children exhibited reductions in RMSSD (n = 8/13), pNN50% (n = 7/9) and HF power (n = 14/18), no difference was reported for LF (n = 10/18), while LF:HF ratio was elevated (n = 10/15). HRV changes during childhood are consistent with a marked and progressive increase in cardiac parasympathetic activity relative to sympathetic activity. Obesity disrupts the normal maturation of cardiac autonomic control.

Contents

Abbreviations: BMI, body mass index; HF, high frequency; HRV, heart rate variability; LF, low frequency; LF/HF, the low frequency to high frequency ratio; NN, normal-to-interval; NU, normalised units; pNN50%, proportion of RR intervals differing by > 50 ms from previous RR interval; QIS, Quality index score; RMSSD, square root of the mean of the sum of successive differences; SDANN, standard deviation of 5-minute average RR interval over a 24-hour period; SDNN, standard deviation of all NN intervals; ST, short term; TINN, triangular interpolation of NN interval histogram. normal RR.

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1. Background

Childhood obesity remains a global public health issue (WHO, 2010). Obesity raises the risk of developing chronic cardiovascular and metabolic disorders (Nguyen et al., 2008) and although previously considered as adult conditions their prevalence is on the rise in children (Whincup et al., 2002). Furthermore, once established in childhood these conditions have been reported to track to adulthood (Raitakari et al., 2003; Whincup et al., 2002). Autonomic dysfunction is prevalent in adults with cardiovascular disease and metabolic disorders (e.g., obesity, hypertension, type II diabetes) and contributes to the underlying pathophysiological processes (Abboud et al., 2012). In contrast to the wealth of data concerning the autonomic control of the heart in adult populations, much less work has been conducted in children. Thus, how cardiac autonomic control normally develops during childhood and how this may be affected by pathophysiological conditions, such as obesity, remains incompletely understood.

Since the 1970s several metrics have been developed to quantify the beat-by-beat fluctuations in heart rate (Kleiger et al., 2005; Task Force, 1996). Such indices of heart rate variability (HRV) can provide a valuable non-invasive insight into cardiac autonomic control (Task Force, 1996) and have prognostic utility as an indicator of cardiovascular risk in adult (Dekker et al., 2000; Thayer et al., 2010; Tsuji et al., 1996) and paediatric (Lammers et al., 2010) populations. Indeed, there is strong evidence to suggest that increased cardiac sympathetic drive is arrhythmogenic (Lown and Verrier, 1976), while high levels of cardiac parasympathetic are cardioprotective (Billman, 2006). HRV represents an attractive means of examining how age influences cardiac autonomic control in healthy children. An age-related alteration in HRV might be expected as a consequence of a multitude of mechanisms, including changes in heart rate, respiratory rate, growth and maturation, hormones, arterial baroreflex sensitivity, body composition and life style. For example, heart rate typically falls with childhood age as heart size (e.g., left ventricular mass, stroke volume) increases relative to body size (Batterham et al., 1997; de Simone et al., 1998; Dewey et al., 2008; El-Sheikh, 2005; Fleming et al., 2011; Porges and Furman, 2011), while respiratory frequency also falls between birth and adolescence (El-Sheikh, 2005; Fleming et al., 2011; Porges and Furman, 2011; Williams and Lopes, 2002). However, studies examining the influence of childhood age on cardiac autonomic control in healthy children appear to be largely equivocal and at present this important topic has not been subject to review.

The physiological mechanisms regulating cardiac autonomic activity are complex and multi-factorial. Recent animal studies have identified a clear role for circulating pro-inflammatory cytokines in evoking increases in sympathetic activity (Helwig et al., 2008; Niijima et al., 1991), reducing cardiovagal baroreflex sensitivity (Takagishi et al., 2010) and reducing HRV (Fairchild et al., 2009). Notably, obesity is characterised by low grade inflammation (Rodríguez-Hernández et al., 2013) and both obesity and plasma markers of inflammation are associated with impairments in cardiac autonomic function in adults (Soares-Miranda et al., 2012; Thayer et al., 2010; Thiyagarajan et al., 2012). In contrast to the extensive work conducted in adult populations, the effect of weight status on HRV in children remains less well understood.

Given this background the purpose of this review is to determine how childhood age influences autonomic control of the heart as assessed using HRV analysis, and determine whether there is sufficient evidence to identify how this may be modified by weight status.

2. Method

The review protocol was carried out in accordance with the Centre for Reviews and Dissemination guidelines (2008).

2.1. Review question and inclusion criteria

This review has two main objectives:

Objective 1 Determine how childhood age influences HRV.
Objective 2 Determine whether there is sufficient evidence to identify how weight status and body composition affect HRV in children.

In accordance with the UN convention (UNICEF, 1989) a child was defined as an individual under the age of 18 years. Studies were included only if participants had no history or symptoms of cardiovascular, pulmonary, metabolic, or neurological disease and were not taking over the counter or prescribed medication. Studies assessing age were included if they compared children of different ages, while those which made comparisons between a group of children and a group of adults were excluded. Adults were excluded for the reason that the focus of the review was to understand how cardiac autonomic control changes explicitly throughout childhood. Only studies which employed an objective measure of weight status (e.g., body mass index [BMI], waist circumference) or a measure of body fat percentage (e.g., skinfold measures, dual-energy X-ray absorptiometry) were included.

Studies which assessed at least one index of HRV measurement in accordance with the guidelines provided by the Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology (1996) were included. Both short-term (2–5 min) and long-term (24 h) indices of HRV were used to provide an indication of overall HRV, and the components associated with cardiac parasympathetic or sympathetic activity. Assessments of overall HRV included SDNN (standard deviation of all RR [NN] intervals), SDANN (standard deviation of 5-minute average RR interval over a 24-hour period), HRV triangular index (total number of NN intervals divided by the number of NN intervals in the modal bin of the NN interval histogram) and TINN (baseline width of the NN interval histogram measured as a base of a triangle). Cardiac parasympathetic activity was evaluated using RMSSD (square root of the mean of the sum of successive differences), pNN50% (proportion of RR intervals differing by >50 ms from previous RR interval) and power spectral density at the high frequency range (HF, 0.15–0.4 Hz) (Malliani et al., 1991; Pagani et al., 1997; Task Force, 1996). Power spectral density at the low frequency range (LF, 0.04–0.15 Hz) was used as a composite index of cardiac sympathetic and parasympathetic activity (Malliani et al., 1991; Pagani et al., 1997; Task Force, 1996), and the LF:HF ratio used to provide an evaluation of the relative contribution of the sympathetic and parasympathetic components to the autonomic control of the heart rate (Pagani et al., 1997; Task Force, 1996). However, it is acknowledged that the use of ratio between LF and HF power spectral density as an estimate of the so-called 'sympathovagal balance' has been questioned, and that a satisfactory