Heart Rate Variability in Irritable Bowel Syndrome

Subjects: Cardiac & Cardiovascular Systems | Gastroenterology & Hepatology Contributor: Magdalena Mróz , Marcin Czub , Anna Brytek-Matera

Heart Rate Variability (HRV) is a non-invasive biomarker that can measure autonomic tone. Autonomic Nervous System deregulation is considered the leading cause of Irritable Bowel Syndrome (IBS), which is associated with decreased parasympathetic tone. HRV can measure the parasympathetic tone and changes in autonomic tone caused by therapeutic intervention in IBS. Further research is needed to confirm the efficacy of using HRV to measure the effectiveness of therapeutic interventions in IBS.

Heart Rate VariabilityIrritable Bowel SyndromeAutonomic Nervous Systembiomarker

vagally mediated HRV

brain-gut axis

1. Heart Rate Variability

Heart Rate Variability (HRV) as an indicator of parasympathetic nervous system activity is widely studied in psychophysiology^{[1][2]}. The parasympathetic nervous system is mainly based on bi-directional communication running through the vagus nerve^[3]. Therefore, the research describes it with the term *vagally mediated heart rate variability* (vmHRV)^{[4][5]}. HRV reflects the body's ability to adapt to psychological and environmental challenges^{[6][7]}.

HRV is the heart's sinus rhythm variability, expressed by differences in the duration of consecutive heart cycles (i.e. the duration of RR intervals)^[1]. The changes in the time between consecutive heartbeats are generated by the heart-brain interactions and non-linear, dynamic Autonomic Nervous System processes, which influence the heart's sinus node. Depending on autonomic nervous system (ANS) activity, gas exchange, blood pressure, heart, gut and vascular tone - the sinus node creates an electrical pulse, which generates the rhythm of the heartbeat^{[1][6]}.

Depending on the type of measurement, HRV can also provide information on sympathetic tone. The "gold standard" for clinical HRV assessment (and also the assessment of sympathetic activity) is 24 hours recordings which take into account metabolism, circadian rhythms, the sleep cycle, core body temperature and the renin–angiotensin system^[9].

Other physiological meanings have short-term (5-minute) measurements from which parasympathetic activity can be assessed (vmHRV). HRV short-term measures are generated by the dynamic relationship between the

parasympathetic and sympathetic branches and the regulatory mechanisms that control heart rate (rhythmic changes in vascular tone, respiratory sinus arrhythmia, and the baroreceptor reflex)^{[1][6]}.

HRV is a non-invasive, pain-free biomarker which is easily approachable. HRV used to be assessed from electrocardiography (ECG) signals^[1]. Currently, it can also be measured by photoplethysmography (PPG)^[10]. ECG or PPG signals can be derived from chest^[11] or finger^{[12][13]} sensors. Depending on the chosen measurement tool, compatible software is required to convert the measurement data into interpretable indices. There are three types of measurement data: time-domain measures, frequency-domain measures and HRV non-linear measures. An overview of widely-used HRV metrics was detailed by Shaffer & Ginsberg^[6]. In addition, Laborde et al. developed recommendations to guide the planning of HRV measurements. It is especially worth noting the standards of measurement conditions, preparation for measurement and the confounding variables influencing HRV that should be controlled^[3].

2. Heart Rate Variability in Irritable Bowel Syndrome

Irritable Bowel Syndrome (IBS) is a functional gastrointestinal disorder, and the disorder of gut-brain interactions is considered its leading cause^[14]. IBS patients experience chronic abdominal pain, intractable diarrhoea, and/or constipation. Experiencing abdominal pain or discomfort associated with IBS symptoms reduces daily work productivity^[15] and increases food avoidance and health worries^[16]. It may exacerbate symptoms of anxiety and somatic, or mood disorders^{[17][18]}.

In IBS the disturbed autonomic balance is characterized by a reduced vagal tone and reduced parasympathetic nervous system activity^{[19][20][21]}. Under the influence of stress, the activity of the vagus nerve decreases (decrease of parasympathetic activity), which causes dysbiosis and increases the secretion and permeability of the intestines. Bonaz et al.^[22] indicate that it increases inflammation in the intestines. Afferent nociceptors become more sensitive, which increases visceral pain sensation in IBS^[23]. In IBS, visceral nociception is also intensified due to functional and structural changes in the brain, immune, and neuroendocrine pathways^[24].

A recent meta-analysis comparing HRV measurements in individuals with IBS with healthy controls at rest has shown some evidence of an association of HRV with gastrointestinal disorders, evidenced by decreased HF (high-frequency band) relative to healthy controls^[25]. Another meta-analysis^[26] has shown that patients with IBS had a lower HF band power compared with healthy controls. Both meta-analyses have found that the analysis of HRV data collected from short-term recordings demonstrated significant differences between IBS and healthy controls, which haven't been observed undergoing 24-h monitoring^{[25][26]}.

Regarding the leading cause of IBS - indicators that may assess changes in parasympathetic activity during 5minute recordings are in the time domain: RMSSD (root mean square of successive RR interval differences) and pNN50 (percentage of successive RR intervals that differ by more than 50 ms), and in the frequency domain: HF (high-frequency band)^{[3][6]}. The HF indicator, as a measure of vagal tone, is sensitive to changes in respiratory rate. Malik et al.^[1] indicated that HF reflects the vagus nerve tone when the respiratory rate is between 9 and 24 breaths per minute (0.15–0.40 Hz). When the respiratory rate exceeds these ranges, it is recommended to assess the RMSSD indicator, which is less sensitive to changes in respiratory rate^[27].

Previously, the most common analysis of inter-individual differences in HRV in IBS has been based on a single measurement of HRV at rest^{[25][26][28][29]}. However, comparisons of intra-individual changes (repeated measurement of resting HRV in the same individual) were made to assess autonomic changes due to postprandial symptoms^[30]. The use of HRV measurements as measures of therapy effectiveness is increasingly being used in clinical trials^{[11][31][32][33][34][35][36]}.

The obtained data are compared to assess changes in resting HRV between two measurements taken in the same individual. This data comparison method is recommended in HRV methodology due to the exclusion of interindividual differences. However, while planning an experiment with a within-subject design, it is necessary to provide comparable conditions over both measurements (the same time of the day)^[3].

To assess the body's ability to adapt to difficult situations, it is also recommended to assess the reactivity of HRV^[37]. This methodology has already been used as part of the assessment of the effectiveness of IBS therapy^[38]. The assessment of changes in HRV reactivity under the influence of therapeutic interventions is interesting from the point of view of assessing changes in the adaptability to environmental challenges at the physiological level. An evaluation of HRV reactivity and resting HRV in the same study may bring additional values to the interpretation of the observed phenomena.

From the perspective of patients with IBS, it is particularly important to control the use of antidepressants due to the significant co-occurrence of depression and IBS. In addition, antidepressants are used for the symptomatic treatment of IBS^{[39][40][41]}. Due to the increased prevalence of IBS among women, it is also advisable to control oral contraceptives and the menstrual cycle phase^{[42][43]}. Due to the sensitivity of short-term HRV measurements to the effects of the body's daily cycle, it is recommended to perform measurements at the same time of the day (and this applies to both inter- and intra-individual measurements).

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