Heart Rate Variability in Irritable Bowel Syndrome

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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.

Keywords: Heart Rate Variability ; Irritable Bowel Syndrome ; Autonomic Nervous System ; biomarker ; 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][8].

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 5-minute 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 inter-individual 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).

References

1. Task Force Of The European Society Of Cardiology The North American Society Of Pacing Electrophysiology; Heart Rate Variability. *Circulation* **1996**, *93*, 1043-1065, 10.1161/01.cir.93.5.1043.
2. Gary G. Berntson; J. Thomas Bigger; Dwain L. Eckberg; Paul Grossman; Peter G. Kaufmann; Marek Malik; Haikady N. Nagaraja; Stephen W. Porges; J. Philip Saul; Peter H. Stone; et al. Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology* **1997**, *34*, 623-648, 10.1111/j.1469-8986.1997.tb02140.x.
3. Sylvain Laborde; Emma Mosley; Julian F. Thayer; Heart Rate Variability and Cardiac Vagal Tone in Psychophysiological Research – Recommendations for Experiment Planning, Data Analysis, and Data Reporting. *Frontiers in Psychology* **2017**, *08*, 213, 10.3389/fpsyg.2017.00213.
4. Elisabet Kvadsheim; Lin Sørensen; Ole B. Fasmer; Berge Osnes; Jan Haavik; DeWayne P. Williams; Julian F. Thayer; Julian Koenig; Vagally mediated heart rate variability, stress, and perceived social support: a focus on sex differences.

Stress **2022**, *25*, 113-121, 10.1080/10253890.2022.2043271.

5. Valentin Magnon; Guillaume T. Vallet; Amanda Benson; Martial Mermillod; Pierre Chausse; Adeline Lacroix; Jean-Baptiste Bouillon-Minois; Frédéric Dutheil; Does heart rate variability predict better executive functioning? A systematic review and meta-analysis. *Cortex* **2022**, *155*, 218-236, 10.1016/j.cortex.2022.07.008.
6. Fred Shaffer; Jp (Jack) Ginsberg; An Overview of Heart Rate Variability Metrics and Norms. *Frontiers in Public Health* **2017**, *5*, 258-258, 10.3389/fpubh.2017.00258.
7. Stephen W. Porges; The polyvagal perspective. *Biological Psychology* **2007**, *74*, 116-143, 10.1016/j.biopsycho.2006.06.009.
8. Julian F. Thayer; Fredrik Åhs; Mats Fredrikson; John J. Sollers; Tor D. Wager; A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience & Biobehavioral Reviews* **2011**, *36*, 747-756, 10.1016/j.neubiorev.2011.11.009.
9. Shaffer, F.; McCraty, R.; Zerr, C.L. A Healthy Heart Is Not a Metronome: An Integrative Review of the Heart's Anatomy and Heart Rate Variability. Front. Psychol. 2014, 0, 1040, doi:10.3389/FPSYG.2014.01040.
10. Vala Jeyhani; Shadi Mahdiani; Mikko Peltokangas; Antti Vehkaoja; Comparison of HRV parameters derived from photoplethysmography and electrocardiography signals. *2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* **2015**, *2015*, 5952-5955, 10.1109/embc.2015.7319747.
11. Mary Katherine Jurek; Hannah Seavey; Meredith Guidry; Emily Slomka; Stacy D. Hunter; The effects of slow deep breathing on microvascular and autonomic function and symptoms in adults with irritable bowel syndrome: A pilot study. *Neurogastroenterology & Motility* **2021**, *34*, e14275, 10.1111/nmo.14275.
12. Ivan Liu; Shiguang Ni; Kaiping Peng; Happiness at Your Fingertips: Assessing Mental Health with Smartphone Photoplethysmogram-Based Heart Rate Variability Analysis. *Telemedicine and e-Health* **2020**, *26*, 1483-1491, 10.1089/tmj.2019.0283.
13. George P. Chrousos; Nektaria Papadopoulou-Marketou; Flora Bacopoulou; Mariantonietta Lucafò; Andrea Gallotta; Dario Boschiero; Photoplethysmography (PPG)-determined heart rate variability (HRV) and extracellular water (ECW) in the evaluation of chronic stress and inflammation. *Hormones* **2022**, *21*, 383-390, 10.1007/s42000-021-00341-y.
14. Douglas A. Drossman; Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features, and Rome IV. *Gastroenterology* **2016**, *150*, 1262-1279.e2, 10.1053/j.gastro.2016.02.032.
15. Åshild Faresjö; Susanna Walter; Anna-Karin Norlin; Tomas Faresjö; Michael Jones; Gastrointestinal symptoms - an illness burden that affects daily work in patients with IBS. *Health and Quality of Life Outcomes* **2019**, *17*, 1-7, 10.1186/s12955-019-1174-1.
16. Pierre Paré; James Gray; Sy Lam; Robert Balshaw; Shideh Khorasheh; Martin Barbeau; Suzanne Kelly; Christopher R. McBurney; Health-related quality of life, work productivity, and health care resource utilization of subjects with irritable bowel syndrome: Baseline results from logic (longitudinal outcomes study of gastrointestinal symptoms in Canada), a naturalistic study. *Clinical Therapeutics* **2006**, *28*, 1726-1735, 10.1016/j.clinthera.2006.10.010.
17. Mihaela Fadgyas-Stanculete; Ana-Maria Buga; Aurel Popa-Wagner; Dan L Dumitrascu; The relationship between irritable bowel syndrome and psychiatric disorders: from molecular changes to clinical manifestations. *Journal of Molecular Psychiatry* **2014**, *2*, 1-7, 10.1186/2049-9256-2-4.
18. Åshild Olsen Faresjö; Ewa Grodzinsky; Claes Hallert; Toomas Timpka; Patients with irritable bowel syndrome are more burdened by co-morbidity and worry about serious diseases than healthy controls- eight years follow-up of IBS patients in primary care. *BMC Public Health* **2013**, *13*, 832-832, 10.1186/1471-2458-13-832.
19. Sonia Pellissier; Cécile Dantzer; Laurie Mondillon; Candice Trocme; Anne-Sophie Gauchez; Véronique Ducros; Nicolas Mathieu; Bertrand Toussaint; Alicia Fournier; Frédéric Canini; et al. Relationship between Vagal Tone, Cortisol, TNF-Alpha, Epinephrine and Negative Affects in Crohn's Disease and Irritable Bowel Syndrome. *PLOS ONE* **2014**, *9*, e105328, 10.1371/journal.pone.0105328.
20. Sonia Pellissier; Cécile Dantzer; Fréderic Canini; Nicolas Mathieu; Bruno Bonaz; Psychological adjustment and autonomic disturbances in inflammatory bowel diseases and irritable bowel syndrome. *Psychoneuroendocrinology* **2010**, *35*, 653-662, 10.1016/j.psyneuen.2009.10.004.
21. Bruno Bonaz; Valérie Sinniger; Sonia Pellissier; The Vagus Nerve in the Neuro-Immune Axis: Implications in the Pathology of the Gastrointestinal Tract. *Frontiers in Immunology* **2017**, *8*, 1452, 10.3389/fimmu.2017.01452.
22. Bruno Bonaz; Thomas Bazin; Sonia Pellissier; The Vagus Nerve at the Interface of the Microbiota-Gut-Brain Axis. *Frontiers in Neuroscience* **2018**, *12*, 49, 10.3389/fnins.2018.00049.
23. Isabelle A. M. Van Thiel; Wouter J. De Jonge; Isaac M. Chiu; Rene M. Van Den Wijngaard; Microbiota-neuroimmune cross talk in stress-induced visceral hypersensitivity of the bowel. *American Journal of Physiology-Gastrointestinal and Li*

ver Physiology **2020**, *318*, G1034-G1041, 10.1152/ajpgi.00196.2019.

24. Sigrid Elsenbruch; Abdominal pain in Irritable Bowel Syndrome: A review of putative psychological, neural and neuro-immune mechanisms. *Brain, Behavior, and Immunity* **2011**, *25*, 386-394, 10.1016/j.bbi.2010.11.010.
25. Adam Sadowski; Corina Dunlap; Alison Lacombe; Douglas Hanes; Alterations in Heart Rate Variability Associated With Irritable Bowel Syndrome or Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *Clinical and Translational Gastroenterology* **2020**, *12*, e00275, 10.14309/ctg.0000000000000275.
26. Qing Liu; Er Man Wang; Xiu Juan Yan; Sheng Liang Chen; Autonomic functioning in irritable bowel syndrome measured by heart rate variability: A meta-analysis. *Journal of Digestive Diseases* **2013**, *14*, 638-646, 10.1111/1751-2980.12092.
27. LaBarron K Hill; Anne Siebenbrock; Are all measures created equal? Heart rate variability and respiration - biomed 2009.. *Biomedical sciences instrumentation* **2009**, *45*, 71-76, .
28. N. Mazurak; N. Seredyuk; H. Sauer; M. Teufel; P. Enck; Heart rate variability in the irritable bowel syndrome: a review of the literature. *Neurogastroenterology & Motility* **2012**, *24*, 206-216, 10.1111/j.1365-2982.2011.01866.x.
29. Hyo-Jung Park; Heart Rate Variability as a Measure of Disease State in Irritable Bowel Syndrome. *Asian Nursing Research* **2008**, *2*, 5-16, 10.1016/s1976-1317(08)60024-9.
30. Yukari Tanaka; Motoyori Kanazawa; Olafur S Palsson; Miranda A Van Tilburg; Lisa M Gangarosa; Shin Fukudo; Douglas A Drossman; William E Whitehead; Increased Postprandial Colonic Motility and Autonomic Nervous System Activity in Patients With Irritable Bowel Syndrome: A Prospective Study. *Journal of Neurogastroenterology and Motility* **2018**, *24*, 87-95, 10.5056/jnm16216.
31. Hyo Jung Park; Chiyoung Cha; The Effect of Korean Hand Acupuncture on Young, Single Korean Students With Irritable Bowel Syndrome. *Gastroenterology Nursing* **2012**, *35*, 403-414, 10.1097/sga.0b013e318274b1f2.
32. Gee Youn Go; Hyojung Park; Effects of Auricular Acupressure on Women With Irritable Bowel Syndrome. *Gastroenterology Nursing* **2019**, *43*, E24-E34, 10.1097/sga.0000000000000332.
33. Vijaya Kavuri; Pooja Selvan; Ariel Malamud; Nagarathna Raghuram; Senthamil R. Selvan; Remedial yoga module remarkably improves symptoms in irritable bowel syndrome patients: A 12-week randomized controlled trial. *European Journal of Integrative Medicine* **2015**, *7*, 595-608, 10.1016/j.eujim.2015.11.001.
34. Vijaya Kavuri; Pooja Selvan; Alireza Tabesh; Nagarathna Raghuram; Senthamil R. Selvan; Remedial Yoga module improves symptoms of irritable bowel syndrome: Replication in the Wait-list group and sustained improvements at 6 months. *European Journal of Integrative Medicine* **2015**, *7*, 609-616, 10.1016/j.eujim.2015.11.002.
35. Xiaodan Shi; Yedong Hu; Bo Zhang; Wenna Li; Jiande Dz Chen; Fei Liu; Ameliorating effects and mechanisms of transcutaneous auricular vagal nerve stimulation on abdominal pain and constipation. *JCI Insight* **2021**, *6*, 1-18, 10.1172/jci.insight.150052.
36. Aelee Jang; Sun-Kyung Hwang; Nikhil S Padhye; Janet C Meininger; Effects of Cognitive Behavior Therapy on Heart Rate Variability in Young Females with Constipation-predominant Irritable Bowel Syndrome: A Parallel-group Trial. *Journal of Neurogastroenterology and Motility* **2017**, *23*, 435-445, 10.5056/jnm17017.
37. Sylvain Laborde; Emma Mosley; Alina Mertgen; Vagal Tank Theory: The Three Rs of Cardiac Vagal Control Functioning – Resting, Reactivity, and Recovery. *Frontiers in Neuroscience* **2018**, *12*, 458, 10.3389/fnins.2018.00458.
38. Hanna Edebol-Carlman; Martien Schrooten; Brjánn Ljótsson; Katja Boersma; Steven Linton; Robert Jan Brummer; Cognitive behavioral therapy for irritable bowel syndrome: the effects on state and trait anxiety and the autonomic nervous system during induced rectal distensions – An uncontrolled trial. *Scandinavian Journal of Pain* **2018**, *18*, 81-91, 10.1515/sjpain-2017-0153.
39. Gail A. Alvares; Daniel S. Quintana; Ian B. Hickie; Adam J. Guastella; Autonomic nervous system dysfunction in psychiatric disorders and the impact of psychotropic medications: a systematic review and meta-analysis. *Journal of Psychiatry and Neuroscience* **2016**, *41*, 89-104, 10.1503/jpn.140217.
40. Joelle BouSaba; Wassel Sannaa; Michael Camilleri; Pain in irritable bowel syndrome: Does anything really help?. *Neurogastroenterology & Motility* **2021**, *34*, e14305, 10.1111/nmo.14305.
41. Agnieszka Kułak-Bejda; Grzegorz Bejda; Napoleon Waszkiewicz; Antidepressants for irritable bowel syndrome—A systematic review. *Pharmacological Reports* **2017**, *69*, 1366-1379, 10.1016/j.pharep.2017.05.014.
42. Stacy T Sims; Laura Ware; Emily R Capodilupo; Patterns of endogenous and exogenous ovarian hormone modulation on recovery metrics across the menstrual cycle. *BMJ Open Sport & Exercise Medicine* **2021**, *7*, e001047, 10.1136/bmjsem-2021-001047.

43. Anna Wilczak; Katarzyna Marciniak; Michał Kłapciński; Agnieszka Rydlewska; Dariusz Danel; Ewa Jankowska; Relations between combined oral contraceptive therapy and indices of autonomic balance (baroreflex sensitivity and heart rate variability) in young healthy women. *Ginekologia Polska* **2013**, *84*, 915-21, 10.17772/gp/1660.