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Heart Rate Variability: An Index of the Brain–Heart Interaction

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1. Introduction

The autonomic nervous system plays an important role in a wide range of visceral-somatic and mental diseases. Cardiac parameters, particularly heart rate as a physiological measure, are extremely sensitive to autonomic influences. Normally, the activities of the sympathetic and parasympathetic branches of the autonomic nervous system are in dynamic balance indicating healthy and flexible physiological system. The autonomic imbalance – low parasympathetic activity and/or sympathetic overactivity resulting in tachycardia – is common to a broad range of maladaptive conditions and it is associated with the increased risk of cardiovascular adverse outcomes (Friedman, 2007; Porges, 2007; Thayer & Sternberg, 2006).

Heart rate is a widely used and easily determinable measure of cardiac rhythm. In many previous investigations, high heart rate has shown to be associated with increased risk of cardiovascular mortality (Shaper et al., 1993). Reunanen et al. (2000) referred to close association between tachycardia and mortality (from cardiovascular as well as noncardiovascular reasons) in a large adult population study. Thus, high heart rate is considered as a simple significant nonspecific predictor of mortality; and the average heart rate could be used as an important indicator of the organism complex state.

Heart rate control is determined by dynamic interaction of acceleratory sympathetic nervous system activation, and deceleratory parasympathetic nervous system activity resulting in rhythmical oscillations - heart rate variability. Its analysis should represent a noninvasive window into cardiac chronotropic regulation providing then important information about central-peripheral interaction. During this decade the pathomechanisms by which central nervous system modulates cardiac autonomic control in various mental disorders as well as the potential links between emotional/cognitive processes and cardiac activity have drawn increasing interest.

This chapter will be focused on the essential questions related to the heart-brain interaction indexed by the heart rate variability: 1. What is its physiological and psychophysiological background? 2. What methods exist in the heart rate variability analysis? 3. What is the

clinical implication of the stated methods especially in children and adolescents suffering from mental disorders?

2. Heart rate and its variability – a link between the brain and the heart

Average-mean value of the heart rate results from a rather complex interplay. Its value is determined by intrinsic activity as well as the joint modifications of the parasympathetic and sympathetic neurons terminating at sinoatrial node. Importantly, when both cardiac vagal and sympathetic inputs are pharmacologically blocked (e.g. atropine plus propranolol as „double blockade“), intrinsic heart rate (IHR) is higher than the normal resting heart rate; therefore, vagal inhibitory influence is dominant. Additionally, like normal resting heart rate the IHR declines with age and its value is calculated according to the mathematical formula: $IHR = 118,1 - (0,57 \times \text{age})$ (Jose & Collison, 1970).

2.1 Parasympathetic and sympathetic regulation of the heart rate

Parasympathetic innervation of the heart by vagus nerve originates in neurons localized in nucleus ambiguus, dorsal vagal nucleus and in the region between these nuclei (Taylor et al., 1999 and others). Acetylcholine, released by postganglionic parasympathetic terminals at the sinoatrial node, slows the rate of sinoatrial node depolarization and discharge by binding to muscarinic cholinergic receptors and activating a transmembrane potassium channels associated with funny-channels inhibition.

In contrast, sympathetic nerves originate in cervical and stellate ganglia and neurons of these ganglia are under control of sympathetic preganglionic neurons located in intermediolateral nucleus of spinal cord thoracic segments (Kawashima, 2005 and others). Noradrenaline is released by sympathetic terminals on the sinoatrial node and accelerates the sinoatrial node rhythm via β_1/β_2 receptors-mediated second messenger cascade of intracellular signals and activating of funny-channels. In addition to these classic neurotransmitter actions, the chronotropic state of the heart can be modulated by a variety of neuropeptides, such as neuropeptide Y, that appear to be colocalized with conventional neurotransmitters in autonomic terminals (Kukanova & Mravec, 2006; Shine et al., 1994). Interactions between neurons within intracardiac ganglia together with interconnections between individual anatomical and functional elements form the basis for complex nervous network of the heart, also called „heart brain“ (Randall, 2000). Thus, this complex intracardiac nervous system together with dominant extracardiac autonomic activity provides modulation of heart activity on both physiological and pathological conditions (Armour, 1999).

Uijtdehaage & Thayer (2000) have elaborated the problem of accentuated antagonism in the control of human heart rate. Based on animal studies that indicate the accelerative effects of the sympathetic nervous system on heart rate highly depending on the background of vagal activity, the authors used an evaluation of respiratory sinus arrhythmia as an index of cardiac vagal modulation and left ventricular ejection time as a sympathetic chronotropic index. They found that sympathetic heart rate effects were substantially smaller with high levels of vagal tone than with low background vagal activity. Furthermore, vagal effects became progressively stronger despite the increasing background sympathetic activity, demonstrating the predominance of parasympathetic control of the heart rate. This finding

implies that changes in cardiac activity resulting from changes in sympathetic control cannot be interpreted accurately unless concurrent vagal activity is taken into account, as well (Uijtdehaage & Thayer, 2000).

2.2 The concept of sympathovagal balance

As above mentioned, the cardiac neural control is mediated mainly via sympathetic-parasympathetic interactions interconnected from central nervous system to postganglionic endings. In most physiological conditions, the activation of either sympathetic or vagal outflow is accompanied by the inhibition of the other suggesting the concept of sympathovagal balance (Malliani, 2000, as cited in Montano et al., 2009). This reciprocal organization seems instrumental to the fact that sympathetic excitation and simultaneous vagal inhibition, or vice versa, are both presumed to contribute to the increase or decrease of cardiac activity required for various situations. Thus, the autonomic balance oscillates from rest, when homeostatic negative feedback reflexes predominate, to excitatory states (*e.g.* emotion), when central excitatory mechanisms, possibly reinforced by peripheral positive feedback reflexes, are instrumental to the enhanced cardiac performance (Malliani et al., 1991). This continual dynamic excitatory-inhibitory interaction leads to heart rate instantaneous oscillations – heart rate variability (Fig. 1). The heart rate variability then reflects complex and sophisticated cardiac neural chronotropic control as well as an ability of the end-organ (heart) in response to regulatory effects (Calkovska and Javorka, 2008).

Just like the driver of a car can modify the number of rotations per minute of the automobile engine according to the needs for speed and acceleration, heart rate immediately adapts to the basic needs of the body (Aubert & Ramaekers, 1999). This continuous brisk heart rate adaptability is expressed by its beat-to-beat changes – heart rate variability.

Fig. 1. The recording of the beat-to-beat heart rate oscillations in young healthy subject (modified by Javorka et al., 2011)

On the other hand, Paton et al. (2005) presented interesting review regarding the pattern of sympathetic/parasympathetic balance (as analogy to the Chinese philosophy of yin and

yang). Unlike the conventional picture of reciprocal control of cardiac vagal and sympathetic nervous activity, as seen during a baroreceptor reflex, many other reactions involve simultaneous co-activation of both autonomic limbs. Thus, vagal activity may enhance sympathetically mediated tachycardia, or can by itself produce a paradoxical vagally mediated tachycardia. A plausible mechanism for this synergistic interaction includes possible activation of chromaffin or small intensely fluorescent cells in the cardiac ganglia. These cells have abundant vagal innervation and include vesicles containing catecholamines (Levy, 1971). Thus, the paradoxical vagally mediated tachycardia could be due to release of catecholamines from these vesicles contained within the intrinsic cardiac neurones (Horackova et al., 1996, 1999). Moreover, alternative mechanisms might include the releasing of the several neuropeptides as co-transmitters from vagal nerve fibers (e.g. neuropeptide Y) or participation of some sympathetic efferent axons from cardiac vagal nerve (Cheng et al., 1997 and others).

Proper functioning of the sympathetic-parasympathetic dynamic balance at rest as well as in response to various internal/external stimuli is important for organism flexibility, adaptability and health. In contrast, the autonomic imbalance, in which one branch of the autonomic nervous system dominates over the other, is associated with a lack of dynamic flexibility and health. Therefore, the autonomic imbalance typically with sympathetic overactivity associated with parasympathetic hypoactivation, indexed by low heart rate variability, could represent potential pathomechanism leading to increased risk of cardiovascular adverse outcomes and all-cause mortality (Task Force, 1996). In the elderly, some studies showed that higher heart rate variability is stronger indicator of cardiac mortality than decreased heart rate variability. Further studies are needed to confirm these findings and to elucidate their physiologic meaning (de Bruyne et al., 1999).

Modern conceptions based on complexity theory hold with the assumption that organism stability, adaptability, and health are maintained through a dynamic relationship among system elements; in this case, the sympathetic and parasympathetic branches of the ANS (Thayer & Lane, 2000). That is, patterns of organized variability, rather than static levels, are preserved in the face of constantly changing environmental demands. For example, in healthy individuals, average heart rate is greater during the day (higher sympathetic activity), when energy demands are higher, than at night (higher parasympathetic activity), when energy demands are lower. The system has a different energy minimum for daytime and for nighttime. Because the system operates „far from equilibrium“, it constantly searches for local energy minima to reduce the energy requirement of the organism. Consequently, optimal system functioning is achieved via lability and variability in its component processes, whereas rigid regularity is associated with mortality, morbidity and ill health (Ellis & Thayer, 2010).

Final common pathway of the central-peripheral heart rate control should be indexed by heart rate variability; therefore, this point is discussed in the following section.

2.3 Heart-brain interaction indexed by heart rate variability

In 1865 Claude Bernard delivered a lecture at the Sorbonne on the physiology of the heart and its connections with the brain (Bernard, 1867; as cited in Thayer & Lane, 2009). His work denoted the first step to systematically investigate the connections between the heart and the brain (Thayer & Lane, 2009).

The studies concerning the brain-heart connection emphasize the modulation of the cardiac activity by the cortex; thus, an extensive research has been directed to identify the pathway by which this neurocardiac control is achieved (Friedman, 2007; Montano et al., 2009; Thayer & Brosschot, 2005; Thayer & Lane, 2009). Benarroch (1993) has described the central autonomic network as an integrated component of an internal regulation system through which the brain controls visceromotor, neuroendocrine, and behavioural responses that are critical for goal-directed behaviour and adaptability. Structural components of the central autonomic network are found at the level of the forebrain (anterior cingulate; insular and ventromedial prefrontal cortices; central nuclei of the amygdala; paraventricular and related nuclei of the hypothalamus), midbrain (periaqueductal gray matter), and hindbrain (parabrachial nucleus, nucleus of the solitary tract, nucleus ambiguus, ventrolateral and ventromedial medulla, medullary tegmental field). The interplay of sympathetic and parasympathetic (vagal) outputs of the central autonomic network through sinoatrial node produces the complex beat-to-beat heart rate variability indicating a healthy and adaptive organism (Thayer & Lane, 2000). Importantly, the output of the central autonomic network is under tonic inhibitory control via GABAergic neurons in the nucleus of the solitary tract. Furthermore, cardiac autonomic afferents send impulses back to the central autonomic network. Then, the heart rate variability can index central autonomic network output, and likewise reflects visceral feedback to the network (Friedman, 2007; Thayer & Lane, 2000).

The importance of the inhibitory processes related to heart rate vagal control leading to complex beat-to-beat heart rate oscillations as a sign of health was emphasized by some research groups (Friedman, 2007; Thayer & Lane, 2000, 2009 etc.). Thayer (2006) in an excellent review implies that the inhibitory nature of cardiac control can be exhibited at different levels – from peripheral end-organ (heart) to the neural structures that serve to link the prefrontal cortex with heart rate variability. The central autonomic network, characterized by the reciprocally interconnected neural structures, allows the prefrontal cortex to exert an inhibitory influence on subcortical structures associated with defensive behavior and thus allows the organism to flexibly regulate its behavior in response to changing environmental demands (Thayer, 2006). For example, the amygdala, which has outputs to autonomic as well as other regulatory systems, and becomes active during threat/uncertainty, is under tonic inhibitory control from the prefrontal cortex. Thus, under conditions of the threat, the prefrontal cortex becomes hypoactive which is associated with disinhibition of sympathoexcitatory circuits. Importantly, proper functioning of inhibitory processes is vital to the preservation of the integrity of the system and therefore is vital to health. In contrast, the psychopathological states such as anxiety or depression are associated with prefrontal hypoactivity resulting in disruption of the inhibitory control (Thayer, 2006; Thayer & Lane, 2009).

Since heart rate variability originates predominantly from oscillations in vagal neural traffic, mediated by rapid changes in acetylcholine, beat-to-beat analysis of the heart rate time series (discussed in the following section in details) can provide important information about dominant inhibitory parasympathetic component in the heart rate regulation (sympathetic cardiac influence is too slow to produce rapid beat-to-beat changes because of norepinephrine kinetics). Specifically, a series of studies using neuroimaging have provided evidence that activity of the prefrontal cortex is associated with cardiac vagal function evaluated by heart rate variability analysis (Lane et al., 2009). For example, Ahs et al. (2009) concluded that vagal modulation of the heart is associated with activity in striatal as well as

medial and lateral prefrontal areas in patients with social phobia. Another study reported the correlations in the superior prefrontal cortex, the dorsolateral prefrontal and parietal cortices activities with parasympathetic-linked cardiac control indexed by the heart rate variability spectral analysis (Lane et al., 2009). Similarly, Napadow et al. (2008) demonstrated correlations between heart rate variability and the activity in the hypothalamus, cerebellum, parabrachial nucleus/locus coeruleus, periaqueductal gray, amygdala, hippocampus, thalamus and prefrontal, insular and temporal cortices. As such, these objective and sensitive methods confirm the fact that the heart rate variability serves to index central-peripheral autonomic nervous system integration, and consequently, is a psychophysiological marker for adaptive environmental engagement (Porges, 1995, 2009).

3. Heart rate variability: Analysis and clinical implications

Heart rate variability is a physiological phenomenon and its assessment can provide useful information about cardiac autonomic regulatory mechanisms. From the clinical point of view, our research is focused on the application of the heart rate variability analysis using traditional (linear) and novel nonlinear methods, particularly in children and adolescents suffering from mental disorders. Since impaired cardiac neural regulation is associated with increased risk of cardiovascular morbidity, our original findings (presented in the following sections) underscore the importance of future research regarding the autonomic neurocardiac integrity in mental disorders already in children and adolescents.

3.1 Heart rate variability – linear analysis

Heart rate variability is traditionally quantified by linear methods – time and frequency (spectral) domain analysis – providing the information about the heart rate variability magnitude and frequencies (Task Force, 1996). The short-term heart rate variability spectral analysis allows to isolate the faster high frequency respiratory-coupled influences on the heart rate variability (HF-HRV: 0.15-0.4 Hz) from slower sources of the heart rate variability (LF-HRV: 0.04-0.15 Hz). It seems that the oscillations in cardiac sympathetic nerve activity make a minor contribution to the heart rate oscillations at low-frequency component (LF-HRV); and these oscillations are derived mainly from a baroreflex, vagally mediated response to blood pressure Mayer waves (Elghozi & Julien, 2007). In contrast, the high-frequency cardiac rhythms are mediated primarily by vagal innervation of the sinoatrial node reflecting the respiratory sinus arrhythmia - physiological phenomenon characterized by the heart rate increases during inspiration and decreases during expiration. The respiratory sinus arrhythmia mechanisms include central medullary generator, reflexes from the lungs, baroreflexes, chemoreflexes, as well as local mechanisms (stretching of the sinoatrial node etc.). Respiratory sinus arrhythmia is mediated predominantly by fluctuations of vagal cardiac nerve efferent traffic originating in the nucleus ambiguus and therefore provides a noninvasive index of cardiac vagal regulation (Berntson et al., 1997; Yasuma et al., 2004). As interpreted by Porges in his polyvagal theory (1995, 2009), the nucleus ambiguus is considered as an origin of the more recently developed „smart“ vagus to facilitate the complex emotion responses and social behaviour. Two sources of structural evidence link respiratory sinus arrhythmia to emotion. Efferent fibers from the nucleus ambiguus innervate the larynx, an important structure for communication of emotional state through vocalization (Porges, 1995). Also, the nucleus ambiguus fibers are believed to

terminate in the source nuclei of the facial and trigeminal nerves, which facilitate the emotion behaviours of facial expression and vocalization. Recently, along with structural evidence, empirical studies relating respiratory sinus arrhythmia to emotion in humans have accumulated (Frazier et al., 2004). Therefore, the respiratory sinus arrhythmia should be considered as an index of both cardiac vagal and emotional regulation.

Our studies analyzed the respiratory sinus arrhythmia changes using the heart rate variability spectral analysis at the high-frequency band in children and adolescents suffering from selected mental disorders (depressive disorder, attention deficit/hyperactivity disorder). Our original results (published by Tonhajzerova et al., 2009a,b, 2010) will be discussed in the last chapter section.

3.2 Heart rate variability – nonlinear analysis

The physiological cardiac control mechanisms integrated from subcellular to systemic levels operate over multiple time scales. This perpetual control results in the complex oscillations of the heart rate – the measured output signal is characterized by great complexity (Javorka et al., 2011). Recently, nonlinear methods measuring qualitative characteristic of the cardiac time series – i.e. complexity, and other system dynamic features have been shown to be more suitable for a detailed description of heart rate autonomic control system (Javorka et al., 2009; Porta et al., 2009).

Moreover, the central autonomic network, resulting in complex beat-to-beat heart rate variability, has many features of a nonlinear dynamical system: reciprocally interconnected components with the function of positive/negative feedback interactions; a presence of a parallel, distributed pathways which are important to a given response (e.g. the modification of the heart rate by various combinations of sympathetic and parasympathetic activity), including other pathways such as circulating hormones (see Friedman, 2007; Thayer & Lane, 2000). From this point of view, the more complex oscillations mean the more complex and healthier regulation indicating better adaptability of the underlying system. Contrary, different diseases are often associated with the reduced heart rate control network complexity indicating insufficient heart rate adaptation to different requirements. Therefore, the loss of complexity was proposed as a general feature of pathological dynamics (see Baumert et al., 2004).

The quantifying of the heart rate variability by linear methods is not sufficient to characterize the complex dynamics of cardiac time series modulation. Therefore, the new parameters quantifying additional information embedded in the heart rate variability signal were developed. However, the application of traditionally used nonlinear methods (e.g. correlation dimension, largest Lyapunov exponent) is limited to long stationary signals – a condition that is only rarely met in physiology (Schreiber, 1999). Then, new methods with applicability to real biological signals are continuously developed to quantify new aspects of short quasistationary heart rate variability signal with the potential to reveal subtle changes in cardiovascular control system (Aubert & Ramaekers, 1999).

In the case of heart rate variability analysis, entropy measures are therefore used to quantify the complexity of heart rate fluctuations. Firstly, the complexity analysis of heart rate variability was performed by calculation of Approximate Entropy (ApEn) (Pincus, 1995). An improved version of ApEn is a measure of Sample Entropy (SampEn) which quantifies the

irregularity and unpredictability of a time series (see Richman & Moorman, 2000). Since heart rate time series under healthy conditions have a complex spatial and temporal structure with correlations on multiple scales, single-scale based traditional entropy measures, including SampEn, fail to account for the multiple time scales inherent in the physiologic systems dynamics. A meaningful measure of the complexity should take into account multiple time scales. Costa et al. (2002) introduced a new method called Multiscale Entropy Analysis to calculate entropy over multiple scales. Multiscale Entropy Analysis describes the complexity for various time scales of fluctuations within the analysed signal.

In our study (Tonhajzerova et al., 2010), we used novel nonlinear method – symbolic dynamics. Symbolic dynamics is a suitable method for the quantification of cardiac time series complexity independent of its magnitude and a potentially promising tool for short-term heart rate variability assessment (Guzzetti et al., 2005; Voss et al., 2009). The symbolic dynamics concept allows a simplified description of the system dynamics with a limited set of symbols. Consecutive values of heart rate time series/their differences are encoded according to some transformation rules into a few symbols of a certain alphabet. Subsequently, the dynamics of that symbol string are quantified, providing information about various qualitative aspects of heart dynamics. Then, in our study the following parameters from the resulting symbolic time series were evaluated: *normalized complexity index (NCI)* - computed as a measure of the amount of information (corrected for short-term time series) carried by the L -th sample when the previous $L-1$ samples are known. NCI is a measure of the complexity of pattern distribution. It ranges from zero (maximum regularity) to one (maximum complexity). The larger the NCI, the more complex and less regular the time series. Our interest was focused on the evaluation of the patterns with two like variations (2LV, the three symbols form an ascending or descending ramp) and the rates of occurrence of this pattern was indicated as 2LV%. This parameter could be considered as a marker of vagal activity (Porta et al., 2006).

Recently, the application of novel nonlinear methods is associated with increased interest (Bär et al., 2007; Baumert et al., 2009). Our findings (published by Tonhajzerova et al., 2010) will be outlined in the following section.

3.3 Clinical implications of the heart rate variability analysis

Despite the heart rate variability traditional (linear) analysis - extensively utilized in clinical practice, the application of new nonlinear methods is rare, in particular in children and adolescents suffering from mental disorders. Since the childhood and adolescent age-period is important concerning the brain-heart interaction, our findings (presented below) underscore importance of this problem emphasizing the interdisciplinary approach.

3.3.1 Depressive disorder

Mean heart rate: The findings regarding average value of the heart rate in depressive disorder are controversial. We found significantly higher heart rate in adolescent girls suffering from major depression compared to controls (Tonhajzerova et al., 2009b, 2010). In contrast, other authors found no significant differences in heart rate between depressive adolescents and controls (Henje Blom et al., 2010). Interestingly, Clark & Watson (1991) introduced the tripartite model, in which anxiety, not depression, is associated with

physiological hyperarousal reflecting in autonomic hyperactivity and heart rate modifications. Heart rate could be taken as a measure of arousal; the higher heart rate, the higher the arousal level (Greaves-Lord et al. 2007). These authors found higher heart rate in major depression pointing towards relatively high arousal in depression as well as in anxiety. Thus, the idea of hyperarousal in anxiety and not in depression is too simple to reflect more complex reality (Greaves-Lord et al., 2007).

Heart rate variability: Impaired autonomic neural regulation of the heart, characterized by increased sympathetic and/or reduced vagal modulation, is likely an important contributor to the cardiac adverse outcomes associated with major depression (for reviews, see Brown et al., 2009; Carney & Freedland, 2009). Although reduced cardiac vagal modulation is a common finding in adult patients with depression (Kikuchi et al., 2009; Udupa et al., 2007), other studies reported unchanged parasympathetic activity (Bär et al., 2004). It seems that the heart rate variability analysis may contribute to early diagnosis of latent and clinically asymptomatic symptoms of a potential cardiac neural dysregulation associated with depression. However, the adolescence is important age-period regarding the depressive disorder. In early adolescence there is a marked increase in depressive symptoms (Galambos et al., 2004), which have a high expectation to continue into early adult life and adulthood (Lewinsohn et al., 1994; Weissman et al., 1999). Chapman et al. (2010) firstly demonstrated an association between neurocognitive regulation and parasympathetic control of the heart (evaluated by respiratory sinus arrhythmia) in children and adolescents. Thus, the heart and mind may be coordinated in order to facilitate adaptive functioning. It is important to note that the adolescence could be a critical and vulnerable age period due to developmental and brain maturational changes (Thayer et al., 2009; Yang et al., 2007). This makes early adolescence as interesting period for studying the depression because of neurobiological as well as psychological maturation (Bosch et al., 2009).

Fig. 2. Graphic protocol of heart rate variability spectral analysis in healthy subject (left) and depressive patient (right) HF – high-frequency band reflecting respiratory sinus arrhythmia. Reduced high-frequency oscillations refer to lower respiratory sinus arrhythmia indicating impaired cardiac vagal control in the patient with major depression. PSD - power spectral density (ms^2/Hz) (modified by Tonhajzerova et al., 2011).

From this point of view, our original findings revealed reduced cardiac time series magnitude indicating impaired neurocardiac regulation already in girls with major depression before treatment (Fig. 2). Interestingly, we found lower complexity of the cardiac time series in a supine position and standing position in the same major depression group (Tonhajzerova et al., 2010). Reduced complexity in heart rate time series is believed to result from a lessened ability of regulatory subsystems to interact (Porta et al., 2007) resulting in maladaptation of physiological system. These findings indicate impaired complex neurocardiac heart rate control in the adolescent girls with major depression before treatment (Tonhajzerova et al., 2010).

Potential mechanisms: The mechanisms of cardiac neural regulation impairment in major depression are still discussed. Thus, it is important to refer to the inhibitory processes described in above-mentioned sections: the prefrontal cortex and its abnormalities (*e.g.* prefrontal hypoactivity) could play a critical role in cardiac autonomic dysregulation associated with major depression because of the failure of the prefrontal cortex to inhibit the amygdala as a region regulating cardiovascular and autonomic responses (Thayer & Lane, 2009). Moreover, other factors participating on abnormal neurocardiac modulation could involve behavioral or lifestyle factors associated with major depression, *e.g.* lack of physical activity. This association is questionable: Uusitalo et al. (2004) found that low-intensity regular exercise training did not prevent heart rate variability from decreasing. Additionally, depressive disorder often overlaps with anxiety. Trait anxiety may moderate the relationship between cardiac vagal regulation and depression, with which anxiety is often associated. For example, low vagal heart rate control was found only in high-anxious subset of the depressive patients (Watkins et al., 1999). In this regard, the reduced vagal modulation of the heart in depression could represent a chronic, consolidated anxiety-related response to everyday aggravations (Berntson et al., 2004).

3.3.2 Attention deficit/hyperactivity disorder (ADHD)

Mean heart rate: Despite the internalizing disorders, the externalizing disorders (ADHD/oppositional defiant disorder-ODD/conduct disorders-CD) are characterized by autonomic underarousal including lower heart rate (Beauchaine, 2001). Generally, low heart rate is considered as a biological marker for externalizing disorders spectrum (see review Ortiz & Raine, 2004), and other authors suggest that low heart rate is a marker of resilience to the effects of environmental challenges in early adolescence (Oldehinkel et al., 2008). The other authors found a tendency towards higher heart rate level in the comorbid ADHD group (ADHD+ODD/CD) in comparison with the heart rate level of the ADHD group (van Lang et al., 2007). These authors suggest that a potential dominance of the parasympathetic activity over the sympathetic nervous system could be more prominent in children with ADHD than in patients with comorbid ODD/CD. Interestingly, the other study revealed tachycardia in children with ADHD in comparison with controls; importantly, this tachycardia was observed during day and night. Nocturnal tachycardia in this group could not be explained by nocturnal activity levels or comorbid externalizing/internalizing problems (Imeraj et al., 2011). These conclusions are consistent with our findings of tachycardia in the children suffering from ADHD-combined type (Tonhajzerova et al., 2009a). The question related to heart rate and ADHD without comorbidities is still discussed.

Heart rate variability: Regarding the autonomic nervous system changes in externalizing psychopathology, each branch can function somewhat independently of the other, therefore, inferences concerning sympathetic or parasympathetic activation based on mean heart rate alone are questionable (Berntson et al., 1994). For example, Mezzacappa et al. (1997) reported lower heart rate and reduced respiratory sinus arrhythmia (as an index of cardiac vagal modulation) in the antisocial group in comparison with controls indicating concurrent sympathetic and parasympathetic dysregulation. Crowell et al. (2006) compared autonomic profiles of preschool children with ADHD and ODD with controls using heart rate variability spectral analysis at high frequency as an index of respiratory linked-cardiac vagal control. Children with ADHD and ODD were not significantly different in baseline respiratory sinus arrhythmia, but authors referred to a potential impaired cardiac vagal regulation in later age-period related to emotion dysregulation and lability. Our original findings indicated tachycardia associated with decreased cardiac vagal modulation in a supine position as well as during active orthostatic test in boys with ADHD (Tonhajzerova et al., 2009a). Beauchaine (2001) referred to reduced respiratory sinus arrhythmia, indicating altered cardiac vagal control, as a potential marker of the dysregulated emotional states. It seems that emotional maturation should represent an important factor connected to parasympathetic-linked cardiac activity; thus, it is questionable whether our findings are related to the features of the ADHD (e.g. emotional immaturity) or the reflection of subclinical abnormal dynamic activation of the autonomic nervous system in response to posture change in children with ADHD (Tonhajzerova et al., 2009a).

Potential mechanisms: As internalizing disorders, the deficit in frontal functioning connected to limbic system and consequent alteration of baroreflex function as well as the modifications in a network of brain regions are proposed in the ADHD-linked cardiac neural dysregulation (Borger et al., 1999). Additionally, we assume that the study of the relevant neurotransmitter's systems, genetic and other factors will be important for a better understanding of ADHD and cardiac autonomic dysregulation in children with ADHD.

4. Conclusion

Although a lack of sensitive heart rate autonomic control likely reflects impaired cardiac nervous system regulation, the sophisticated brain-heart interactions are incompletely understood. Importantly, cardiac neural dysregulation is associated with the increased risk of cardiovascular morbidity. This chapter tried to summarize the importance of the identifying of neurocardiac control changes reflecting in complex heart rate time series variability, as an index of the central-peripheral interactions, using conventional (linear) as well as nonconventional (nonlinear) methods. Our findings revealed decreased magnitude and complexity of heart rate time series indicating altered neurocardiac regulation in children and adolescents suffering from selected mental disorders (ADHD, major depression) without pharmacotherapy (Tonhajzerova et al., 2009a,b; Tonhajzerova et al., 2010). From the point of clinical utilization, the heart rate variability analysis by both traditional and novel methods might provide important insight into complex cardiac autonomic regulation in children and adolescents with mental disorders. Further research on cardiac autonomic function in ADHD, major depression and other mental disorders is necessary.

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Tachycardia

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Heart rates are normally controlled by a natural pacemaker, the sinus node, and normal heart rhythm is called sinus rhythm. Tachycardia is defined as a faster heart rhythm than normal sinus rhythm. Tachycardias can cause symptoms such as palpitations, chest pain, shortness of breath and fatigue, which reduce the quality of life. Fast tachycardias can cause hemodynamic collapse and sudden cardiac death. The causes, mechanisms, and origins of tachycardias are various. The diagnosis of tachycardias is made by electrocardiograms and electrophysiological testing. Tachycardias can be managed and treated by pharmacological and non-pharmacological approaches. This book covers these concerns from basic and clinical points of view and will lead to a further understanding and improvement in the clinical outcomes of tachycardias.

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