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HEART RATE VARIABILITY

A Possible Measure of Subjective Wellbeing?

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Abstract

Wellbeing and subjective wellbeing (SWB) has become some the most important goals of our time, both individually and societally. Thus, there is a need for reliable ways to measure SWB, as concerns regarding many current measures have been raised. Due to the interwoven nature of physiology and psychology, heart rate variability (HRV) has the potential to assess psychological processes in a physiological manner. HRV is an attractive measure since it is inexpensive, easy and non-invasive. Hence, the aim is to, from a cognitive neuroscientific standpoint, investigate whether HRV could serve as an objective measure to assess SWB. Most studies demonstrate associations between HRV and SWB, in particular between high frequency (HF)-HRV and positive affect (PA). However, the one study fully matching the theoretical framework only showed an inverse correlation between HRV and negative affect (NA). Plausibly implying that HRV does not serve as a reliable measure of SWB, but may be able to indicate inverse associations with NA, and possibly index certain aspect of SWB such as deactivated PA. The study of the relationship between HRV and SWB is still in its infancy and results are inconsistent. The lack of common standards regarding measurements, implementation details, and variable values, make results difficult to compare and generalize. Further standardizations and research are much needed before accurate conclusions can be drawn.

Keywords: heart rate variability, HRV, subjective wellbeing, measurement, cognitive neuroscience

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Heart Rate Variability: A Possible Measure of Subjective Wellbeing

In the contemporary Western world, increasing wellbeing (WB) has become one of the most important goals on both an individual and societal level (Lyubomirsky & Lepper, 1999). It is a main objective for the World Health Organization (Lindert, Bain, Kubzansky, & Stein, 2015) and listed on third place on the United Nations sustainable development goals for 2030, stating the importance of ensuring healthy lives for all and to promote WB for all people in all ages (United Nations, 2015). The topic of WB has been widely debated and documented: from ancient Greece philosophers such as Aristotle, to present day politicians, philosophers, and laymen as well as in popular psychological magazines and books (Lyubomirsky & Lepper, 1999). Even though diverging opinions exists, a general agreement among scientists is that WB refers to the optimal psychological experience and functioning of an individual (Ryan & Deci, 2001). Current WB research is typically divided into two major approaches; hedonic or subjective wellbeing (SWB), and eudaimonic or psychological wellbeing (PWB) (Diener, 1984; Linley, Maltby, Wood, Osborne, & Hurling, 2009; Ryan & Deci, 2001), with most scientific consensus regarding the concept of SWB (Waterman, 2008).

The apparent importance of the topic calls for a reliable and valid way of measuring it. However, when it comes to assessing WB and in particular SWB and its different aspects, the most commonly used measurement is self-report scales. These can sometimes be limiting, with problems such as: social desirability (Diener, 2000), cultural differences in regard of definitions and evaluations (Lu & Gilmour, 2006), different interpretations of response categories (Kahneman & Krueger, 2006), and when facing new perspectives since self-reports do not include participants' own comments (Delle Fave, Brdar, Freire, Vella-Brodrick, & Wissing, 2011). Hence, one of the great challenges in WB research has been to measure this construct (Tov, 2018). Diener (2000) stresses the need for additional methods, enabling WB assessment through, for instance, physiological measurements.

Because of the interwoven nature of physiology and psychology, heart rate variability (HRV) has been recognized as a potential tool to measure psychological processes through physiological processes (Berntson et al., 1997) and, hence, get around the subjective biases from self-reports. HRV describes the beat-to-beat variation in heart rate and represents the varying change in time between consecutive heartbeats; a variation largely affected by the autonomic nervous system with complex interactions between the parasympathetic and sympathetic systems (Billman, 2011). High frequency (HF) HRV has gone from only being an indicator of parasympathetic nervous system functioning to recently being recognized as an indicator of other functions as well, including emotion regulation and psychosocial functioning (Sloan et al., 2017). The measures are easy to perform, inexpensive and non-invasive, making it an attractive test (Acharya, Joseph, Kannathal, Lim, & Suri, 2006). However, there is to date no scientific review of the connection between WB (or SWB) and HRV.

The aim of this thesis is to investigate the existing cognitive neuroscience literature on HRV and SWB, respectively. In particular, I review whether HRV is a reliable method for the objective measurement of SWB.

In order to answer this question this thesis will be divided into three parts. I begin by providing an overview of WB, including common definitions of it. I subsequently focus on SWB, which is the chosen focus due to the greater scientific consensus regarding definitions of the construct. I further present associated neural correlates and measurement methods. In the second part, I introduce HRV and explore biological underpinnings. In particular, the autonomic nervous system, neural correlates, and associated neural theories, after which I present measurements of HRV. In the last part, I present and examine current studies on HRV in relation to SWB, based on the theoretical framework presented in the first two parts. I close the thesis with a discussion and limitations of current research and provide further directions in the area. The discussion end with a conclusion of the central findings, proposing that HRV might be able to indicate some particular aspects of SWB, but not the construct as a whole. I further conclude that additional standardizations are needed before accurate conclusions can be drawn on the reliability of HRV as a measure of SWB. Moreover, due to the limited scope, this thesis will focus on the literature of HRV related to SWB or aspects of the construct, and not report all existing literature on HRV, which largely concern physiological illnesses and the biology of the heart.

Wellbeing (WB)

Wellbeing (WB) have been actively debated since ancient Greece (Henderson & Knight, 2012), resulting in many theories and attempts to define it through different conceptualizations and interpretations (Dodge, Daly, Huyton, & Sanders, 2012). The vast variety of perspectives and the absence of a systematic or unified overview, challenges empirical investigation on WB (Huta & Waterman, 2013). A great contribution to these challenges was, however, when positive psychology was established as a subfield within psychology in 1998, specifically investigating WB, character strengths, and quality of life (Seligman & Csikszentmihalyi, 2000). Although many new interventions, theories, and constructs have been developed within this subfield, researchers within positive psychology have primarily investigated WB from two perspectives: the hedonistic viewpoint and the eudemonic viewpoint. This general division of WB tends to be used by the majority of today's researchers (Ryan & Deci, 2001). In the Nicomachean Ethics, the fourth-century philosopher Aristotle was the first to make this division as he made the distinction between living the good life (eudaimonia) and pleasure (hedonia) (Kashdan, Biswas-Diener, & King, 2008).

Eudaimonia has been defined as engagement in the existential trials of life and living in accordance with one`s values and has its focus on psychological WB (Ryan & Deci, 2001).

There are however a broad range of constructs associated with eudaimonia, including the seven following: (a) PWB, consisting of high levels of autonomy, personal growth, environmental mastery, purpose in life, self-acceptance and positive relations with others (Ryff, 1989); (b) self-determination and fulfilment of the fundamental human needs of competence, autonomy and belonging (Ryan & Deci, 2001); (c) intrinsic motivation and pursuing goals corresponding to one´s core values and interests (Ryan, Huta, & Deci, 2008); (d) living in harmony with one´s purpose and meaning in life (Seligman, 2002); (e) partaking in activities that evoke engagement, fulfilment and aliveness (Waterman, Schwartz, & Conti, 2008); (f) calmness or vitality, energetic feelings (Nix, Ryan, Manly, & Deci, 1999); (g) and curiosity and openness to novel experiences orienting towards change and personal growth (Kopperud & Vittersø, 2008). Furthermore, eudaimonia has been the foundation of the philosophical objectivist theories of WB, holding the importance of objective values such as friendship, knowledge, and ethics, rather than subjective experiences of, for instance, pleasure (Brülde, 2007). The objectivist approach brings concerns about using subjective reports to assess eudaimonia, since subjective experience doesn't necessarily reflect a life of virtue and excellence (Henderson & Knight, 2012). Consequently, the wide range of definitions of eudaimonia makes both operationalization and research difficult. For example, methodological issues arise when examining the psychometric properties (e.g., the structural validity) of measures of elements of eudaimonia, since it often is unclear what to use as the dependent variable (Kashdan et al., 2008). Moreover, the lack of a common conceptual language results in difficulty to achieve comparable results (Huta & Waterman, 2013).

In comparison to eudaimonia, hedonia includes greater life satisfaction, more positive affect and less negative affect. This approach has its focus on SWB (Diener, 1984; Linley et al., 2009; Ryan & Deci, 2001) which is defined as the cognitive and affective self-evaluation of one´s life (Diener, 2000). The hedonic view has laid the foundation for the philosophical subjectivist theories, emphasizing the importance of the affective, pleasant side of WB (Kashdan et al., 2008), seeing pleasure and pain as useful indicators of what forms a good life (Epicurus, 3rd Century BCE/1987), and as powerful motivators (Bentham, 1789/1988; Hobbes, 1651/1987). The hedonic approach has reached a greater scientific consensus, a more extensive understanding, and has a larger body of research in comparison to the eudaimonic perspectives. A search the 5th of May 2018 on PubMed generates 4304 hits for "hedoni*" and 197 hits for "eudaimoni*". Despite the greater consensus of SWB, there remain challenges. For example, the term happiness is often conflated with SWB (Lyubomirsky & Lepper, 1999).

However, to avoid further conceptual and operational confusion (Dodge et al., 2012; Henderson & Knight, 2012; Huta & Waterman, 2013) the scope of this thesis regarding WB will hereafter be limited to hedonia. This mainly due to the greater scientific consensus (Henderson & Knight, 2012; Waterman, 2008) specifically regarding operational definitions, needed further on in the thesis. From hereafter, hedonia will be referred to as SWB, which is the most commonly used concept in research (e.g., Diener et al., 2017; Hoorn, 2007; Ryan & Deci, 2001) based on Diener`s (1984) notion of hedonia.

Subjective Wellbeing (SWB)

The inception of scientific studies of SWB was partly a reaction towards the alleged overemphasis on pathology in psychological research (Diener, Suh, Lucas, & Smith, 1999). SWB is concerned with the individuals own perception of their life and how well it is going, without particular thought of what it objectively looks like (Tov, 2018). The area of SWB has grown vastly with 46 079 published articles according to PubMed on the 5th of May, 2018.

Consequently, there are different approaches gauging SWB in different ways. According to Kim-Prieto, Diener, Tamir, Scollon, and Diener (2005), three central approaches can be acknowledged. The first recognize SWB as a global evaluation of life and its different aspects. The second approach understands SWB to be a recollection of previous emotional experiences (Kim-prieto et al., 2005). The last approach considers SWB to be an aggregation of manifold emotional reactions over time (Kahneman, 1999).

However, generally SWB is defined as the individual's subjective experience of his or her emotions and thoughts (Diener et al., 1999). It is often considered a broad umbrella term referring to all different types of life evaluations of emotional experiences (Diener et al., 2017), rather than one single specific construct. To comprehend the fullness of the SWB it is important to understand the components both on their own and together as a higher order construct (Diener et al., 1999).

According to Diener et al. (1999), SWB consists of the combination of affective and cognitive perspectives and includes three interrelated components: people's emotional responses, global judgment of life satisfaction and domain satisfaction. People's emotional responses, or affective components, further divide into two aspects: positive affect (PA) and negative affect (NA). PA refers to emotions such as joy, elation, contentment, ecstasy, pride, and happiness, compared to NA that includes sadness, anxiety, anger, depression, guilt and shame (Diener et al., 1999). PA/NA indicates valence, i.e. the degree of pleasantness or unpleasantness. Other major aspects of the affective components are frequency (how often it occurs) versus intensity (how strong it is); and low arousal (for instance calm) versus high arousal (for instance enthusiastic) (Tov, 2018). In contrast, the cognitive components can be described as an evaluative belief about one´s life (Schimmack, 2008) and consists of global judgments of life satisfaction (LS) and domain satisfaction (DS). LS refer to how the individual cognitively evaluates all aspects of one´s life in general. DS, on the other hand, refers to the evaluation of specific domains in the individual`s life, such as satisfaction with marriage, work, finances, self, ones group or health (Diener et al., 1999). It is assumed that the evaluation is done between the desired and current state of life. Moreover, SWB is experienced when pleasure is maximized and pain minimized, that is to say when PA outweighs NA (Diener, 1994).

Furthermore, the cognitive and affective components of SWB have been shown to be distinct, but interrelated constructs (Diener et al., 1999). To a certain extent this is expected; while the affective components often are experienced in relation to a specific event, the cognitive judgment of satisfaction may involve a variety of factors. This can, for instance, be certain standards that are used to compare one`s life against, and to judge how well one think life is going (Tov, 2018). Moreover, the cognitive components tend to be more stable than the affective components, that often are more fluctuating (Eid & Diener, 2004). Hence, the cognitive component may have a stronger association with factors that destabilize or stabilize the general SWB (Tov, 2018). There is, however, contradictions to this assumption, for instance that personality traits correlate more strongly with the affective component (Schimmack, Schupp, & Wagner, 2008), where for example extraverts may be more prone to attend positive stimuli in comparison to introverts (Derryberry & Reed, 1994). Even though there are stable differences in the individual mean level of affect, i.e. in trait (Tov, 2018), SWB seems to be dependent on both state and trait (Eid & Diener, 2004). Stones and Kozma (1986) noticed that SWB appears to act both as a trait and provide long-term stability, and as a state affected by changes in the environment.

Hereafter, the cognitive neuroscientific perspective on SWB will be presented, with main focus on functional findings.

Cognitive Neuroscientific Perspective on SWB. In spite of the long history of research on SWB, it was not until 2004 that the first study, directly and specifically investigating the neural correlates of the concept SWB, emerged (Urry et al., 2004). There are, however, earlier studies investigating aspects of the constructs, primarily affective SWB. Starting with the affective component of SWB, a large body of research using electroencephalographic (EEG) support the understanding that in the experience of affect, the prefrontal cortex (PFC) is asymmetrically involved (e.g., Davidson, Jackson, & Kalin, 2000). Individuals reporting greater dispositional PA and lower dispositional NA show more extreme and stable levels of greater left than right frontal activation (e.g., Tomarken, Davidson, Wheeler, & Doss, 1992). Moreover, tonic left frontal activation is linked to increased PA in response to positive stimuli, and reduced NA in response to negative stimuli (e.g., Wheeler, Davidson, & Tomarken, 1993). Associations between emotional responses and frontal asymmetry have been detected in infants of 4 months and could predict withdrawal or approach behaviour 10 months later (Fox, 1994). Further support can be found in an EEG study investigating the correlation between self-report measures of WB such as Positive and Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1988) and Satisfaction With Life Scale (SWLS; Diener, Emmons, Larsen, & Griffin, 1985) with asymmetrical brain activation (Urry et al., 2004). The results revealed a positive correlation between mentioned SWB measures and greater left than right PFC activation. However, when controlling for variation in dispositional PA, no significant correlation of SWB and left frontal activation was found (Urry et al., 2004).

Moreover, greater activation of left PFC in relation to PA and approach-related emotions have been confirmed by several meta-analyses (e.g., Murphy, Nimmo-Smith, & Lawrence, 2003; Wager, Phan, Liberzon, & Taylor, 2003) In total, individuals with a bias in left frontal asymmetry are more likely to generally show more PA, particularly towards positively valenced stimuli. They also report higher scores on SWB measures, and are more approach than withdrawal oriented in comparison with individuals with right frontal bias (e.g., Coan & Allen, 2004; Tomarken et al., 1992; Wheeler et al., 1993).

Additionally, research in affective neuroscience discovered networks of brain regions activated by pleasant states and events (Kringelbach & Berridge, 2009). These hedonic systems are well developed and covering both cortical and subcortical levels, where brain circuits of more basic hedonic pleasures and higher pleasures seem to overlap (Berridge & Kringelbach, 2011). Findings also indicate that a state of PA includes at least three components of liking, wanting and learning. Liking, which characterizes the actual hedonic impact or pleasure component, but each of the three components is playing a central role in pleasure (Berridge & Kringelbach, 2011). Moreover, these pleasure- networks are widespread but frugal (Kringelbach & Berridge, 2009). Only a few “hedonic hotspots” (identified as liking reactions) has been found, primarily residing in subcortical structures and capable of intensifying liking or hedonic pleasure (Berridge & Kringelbach, 2011). The hotspots are distributed as an interconnected chain across numerous separate deep structures of the brain. One main hotspot has been located in the nucleus accumbens, and another important hotspot in the ventral pallidum (Berridge & Kringelbach, 2011). Notably, these hotspots’ functional neuroanatomy is moderated by neurotransmitters, such as endorphins, which seem to have a specifically strong effect on pleasure or “liking” (Smith & Berridge, 2005). Further hotspots can be found in limbic regions of the PFC and in deep brainstem regions containing the parabrachial nucleus in the pons (Berridge & Kringelbach, 2011).

Beyond already mentioned hotspots, additional regions associated with pleasure include the cortex, specifically orbitofrontal cortex (OFC), which seems to code pleasure in the brain. A zone in the mid-anterior OFC shows specifically strong correlation with conscious subjective pleasantness ratings of for example food, sexual orgasms, and music (Kringelbach & Berridge, 2010). Activity in this region of OFC selectively tracks variations in subjective pleasure and is seen as the primary candidate for coding the subjective experience of pleasure (Kringelbach, 2005). Yet, it is unclear whether the mid-anterior OFC merely codes the state of positive pleasure, or if it can also cause it (Berridge & Kringelbach, 2011). However, Berridge and Kringelbach (2011) emphasize the importance of not over-interpreting the results since there is no established neuroscience of WB.

Additionally, in pleasure (and reward) processing, the role of the mesolimbic dopamine system has been recognized. This system has plentiful connections to the amygdala, PFC, and hippocampus, with dopaminergic projections from the ventral tegmental area to nucleus accumbens (Posner, Russell, & Peterson, 2005).

As for the cognitive aspect, a resting-state fMRI (rs-fMRI) study exploring the neural basis of both the cognitive (SWLS; Diener et al., 1985), and affective (PANAS; Watson et al., 1988) components of SWB, found that the cognitive component was correlated with multiple regions, including a positive correlation with activity in right posterior mid-cingulate cortex (pMCC), superior temporal gyrus (pSTG), left planum temporale (PT), right lingual gyrus, left postcentral gyrus (PCG) and right thalamus (Kong, Hu, Wang, Song, & Liu, 2015). Further, it revealed a negative correlation with e.g. OFC and bilateral SFG. In comparison, the affective component was correlated with a region including the right amygdala. Suggesting that spontaneous brain activity in an emotion-associated region is linked to affective SWB, while regions associated with cognition, sensation, social perception and emotion is linked to cognitive SWB. However, due to the topic still being relatively new, the exact neural correlates underlying SWB are still mostly unknown (Kong et al., 2015).

Measurements of SWB. Measures of SWB are manifold. This has resulted in disagreement regarding what and how to assess it (Kim-prieto et al., 2005). Dodge et al. (2012) argue that as the interest in measuring SWB grows, the greater the necessity for clarity regarding what is being measured, how it should be interpreted, and what assessment techniques should be used. Despite some disagreement, one general understanding originates from the fields history in survey research, making self-report scales (or introspective measures) the most commonly used assessment technique (Diener et al., 1999). Further details on introspective measures and common SWB scales will follow.

Introspective measures. There are various existing introspective measures to use when assessing SWB. Regardless of technique used, it is important to note that the two facets of SWB (affective and cognitive) should be assessed individually. The affective and cognitive aspects have distinct associations with other variables, for example in terms of what influences them and what they influence. The two are also detachable from each other in factor analysis (Diener et al., 2017; Diener et al., 1999). Thus, to fully assess SWB and provide a complete account, several components of the larger construct must be measured (Diener et al., 2017). The affective and cognitive aspects of SWB generally exhibit a positive correlation but appear to differ depending on culture. In more individualistic (e.g., Western) countries a correlation of about $r = .50$ can be seen, whereas in more collectivist (e.g. Asian) countries a correlation of as low as $r = .20$ has been found (Suh, Diener, Oishi, & Triandis, 1998).

As for the affective component constituting of PA and NA, the two are to be seen as distinct dimensions and not as opposites on the same continuum (Dodge et al., 2012). To assess this affective facet, common self-report scales are for example (PANAS; Watson et al., 1988). PANAS consists of a list of 10 positive and 10 negative affect words, where respondents indicate to which amount they have felt the affective state during the last week, using a 5 point scale ranging from “not much at all/very little” to “very much”. The scale has shown to have high test-retest reliability, convergent validity and internal consistency (Thompson, 2007). There are, however, studies showing that PA has different facets that may relate to health and stress differently. For instance, suggesting that the PA items in are high intense items (or activated PA), which further should be divided into three distinct facets of; joy, activation, and interest (Egloff, Schmukle, Burns, Kohlmann, & Hock, 2003).

Additionally, the greatest predictor of SWB regarding the affective experience seems to be the frequency of positive versus negative affect in an individual´s life over time, rather than affect intensity (Larsen, Diener, & Emmons, 1985). Affect intensity is linked to the research within the circumplex model of affect (Russell, 1980), suggesting that affective states result from two different neurophysiological systems. One linked to valence (pleasure-displeasure) and one to arousal (or alertness). Every emotion is seen as a combination of these dimensions of arousal and valence (Posner et al., 2005). The 16-item questionnaire Trimmel's Index of Trait Moods (TRIM-T) is based on the circumplex model of affect, where the subjects rate moods of four dimensions; energy, good mood, motivation and relaxation on a 5-point Likert scale (Trimmel, 2015).

In contrast, the assessment of the cognitive facet of SWB can be done either by asking individuals to evaluate their life by pointing out the best and worst possible life and locate their current life in between (Tov, 2018). Or by asking individuals about their LS, where self-report measures like (SWLS; Diener et al., 1985) or temporal satisfaction with life scale (TSWLS; Pavot, Diener, & Suh, 1998) can be used. SWLS consists of five statements about life satisfaction on which the respondents indicate if they agree or disagree using a 7-point scale (Diener et al., 1985). The TSWL includes an addition of temporal dimensions allowing for assessment of past, present, and future (Pavot et al., 1998).

Moreover, an essential aspect when assessing SWB is through which method it is done (Hoorn, 2007). The Experience Sampling Method (ESM; Scollon, Kim-Prieto, & Diener, 2003) solicit immediate and frequent reports from the partakers in their usual environment, which have important advantages. For instance high ecological validity, avoidance of retrospective distortion, and enabling associations between environmental circumstances and individual affectivity, due to the randomly-timed reports. Further, both reliability and validity increase due to the high-frequency assessment (Hoorn, 2007). ESM is, furthermore, a general approach of measuring and not a specific implementation. For instance, both physiological tests, as well as self-reports such as PANAS, can be used (Hoorn, 2007).

Despite the vast amount of research, there are still many concerns raised regarding current assessments of SWB. For example regarding cultural difference in evaluating and defining SWB (Lu & Gilmour, 2006). The study of SWB has mainly emerged within a Western context that is based on an individualistic self-concept (Markus & Kitayama, 1991). In line with this notion, Lu and Gilmour (2006) found that East-Asians tend to possess greater socially oriented SWB whereas Euro-Americans seems to possess greater individual-oriented SWB (Lu & Gilmour, 2006). Due to these differences, challenges arise when assessing SWB with self-report scales, across cultures. Another potential problem concern that people may respond to self-report scales in ways they perceive as being socially desirable, for example, by reporting more PA than indicated by other assessments (Diener, 2000). Moreover, Kahneman and Krueger (2006) raise concerns about the interpretation of response categories, for example, one respondent may rarely use superlatives and choose a 4 representing “satisfied”, while the other respondent tends to be extreme regarding self-descriptions and instead choose a 6 representing “very satisfied”. Despite these two individual´s different answers, the actual felt satisfaction may be identical.

Diener, (2000) argues that additional methods should be included, such as physiological measurements. Although SWB is subjective by definition, self-reports are not the only way to assess experience, since many experiences also can manifest physiologically (Diener, 2000). A brief overview of some common psychophysiological measures will be presented.

Psychophysiological measures. The use of physiological signals to study psychological phenomena can be done via various methods. The benefits of measuring physiological processes is that they are mostly involuntary (Kivikangas et al., 2011). They are, hence, less contaminated than introspective measures by factors such as interpretation, social desirability, and culture (Diener, 2000; Kahneman & Krueger, 2006; Lu & Gilmour, 2006). However, One way to assess SWB is via neuroimaging methods, for example by correlating self-reports such as PANAS and SWLS with resting-state fMRI (e.g., Kong et al., 2015), or EEG (Urry et al., 2004). However, issues could be raised in regard of the ecological validity using this type of methods where participants need to attend to a laboratory and be physically attached to the equipment, or be inside a machine, which may not be fully transmittable to the experience of WB in daily life (Spooner & Pachana, 2006). Furthermore, sources of error when using fMRI can, for instance, be head, eye, or muscle movement, which might possibly result in false activation patterns (Kimberley & Lewis, 2007).

Another example of more mobile measurements is electrodermal activity (EDA), a measure of skin conductance. EDA has been associated with emotional arousal and is a rather common measure of ANS activity. The responses of EDA are however delayed around 1-3 sec, which aggravates the interpretation of the connection to ANS (Mendes, 2009). They are more mobile than neuroimaging measures, but still require artificial clinical environments and laboratory settings. Due to the absence of sensors that can be worn over longer periods of time and during normal daily activities, the ecological validity gets affected (Poh, Swenson, & Picard, 2010).

Moreover, SWB may also be assessed via biological markers, such HDL cholesterol that has been associated with PA (Ryff, Singer, & Love, 2004), or secretion of oxytocin that has been associated to positive mood (Ryff, Singer, Wing, & Love, 2001). These types of measures tend to be costly and are in isolation not always indicative of the underlying process, many can further only be collected in laboratory settings, affecting the ecological validity, and are temporally associated (Piazza, Almeida, Dmitrieva, & Klein, 2010).

HRV might be an alternative to the above-mentioned methods. HRV has advantages such as being reliable even in an uncontrolled environment, can be used over a longer period of time, is a real time measure, is wearable and portable and does not affect the individual, which enables conduction of studies with high ecological validity investigating real life scenarios (Massaro & Pecchia, 2016).

Heart Rate Variability (HRV)

The first measures of heart rhythm (HR) (using a water clock) were most likely conducted around 335-280 BC by the Greek physician and scientist Herophilus (Billman, 2011). Since then, physicians have intensely tried to study HR (Berntson et al., 1997) and perhaps the most important step was taken when Willem Einthoven in 1901 managed to perform the first electrocardiographic (ECG) recordings of HR and thereby pushed science forward into modernity (Martinez et al., 2017). As a result of such and several more scientific advances, today, we understand a great deal more about HR. For instance, it is agreed upon that HR naturally changes due to circadian rhythms (Kleiger, Stein, & Bigger, 2005), breathing (Bernardi, Porta, Gabutti, Spicuzza, & Sleight, 2001), nervous system influences (Robertson, 2004), baroreflexes, (i.e. homeostatic mechanisms reacting to blood pressure changes), or due to thermoregulation (Berntson et al., 1997). Emotion and exercise also seem to have great effects (Kleiger et al., 2005).

In relation to heart rate variability (HRV), which represents the time variation between two consecutive heartbeats (a more detailed definition will follow), the first documented descriptions are from Stephen Hales in 1733 as he observed respiratory patterns, blood pressure and pulse. HRV has since then been mentioned in several historical studies as a physiologically meaningful measure (Berntson et al., 1997). More recently, through the advancements and availability of digitalized, high-resolution ECG recordings, and fast computers as well as a wide range of methods and algorithms to extract the information concealed in variations of HR (Parati et al., 2006), the relationship between HRV and different psychological and cognitive processes has been studied (Berntson et al., 1997).

Greater HRV is associated with indices of WB such as motivation for social engagement (Kemp et al., 2012), and cheerfulness and calmness (Geisler, Vennewald, Kubiak, & Weber, 2010). Research has also implied that individuals with higher resting HRV have a more adaptive and flexible emotional responding (Thayer, Hansen, Saus-Rose, & Johnsen, 2009), emotional regulation (e.g. Appelhans & Luecken, 2006; Geisler et al., 2010; Thayer & Lane, 2009) emotional expressivity (Butler, Wilhelm, & Gross, 2006) and possess more effective behavioural responses on executive cognitive tasks (Hansen, Johnsen, & Thayer, 2003). In contrast, lower HRV is associated with affective and cognitive dysregulation (Thayer et al., 2009), for example with failing to identify safety cues to novel stimuli (Hansen et al., 2003), and with a harder time to adapt to the environment (Lane et al., 2009; Thayer & Lane, 2009). Individuals with lower resting HRV has been linked to various psychopathologies (Thayer & Lane, 2000), including panic disorders and generalized anxiety disorder (Pittig, Arch, Lam, & Craske, 2013), depression (Rottenberg, Kasch, Gross, & Gotlib, 2002) and schizophrenia (Bär et al., 2008). Additionally, HRV has become widely accepted as a clinical tool for evaluating cardiac autonomic changes in individuals (Billman, 2011; Malik et al., 1996) and is one of the most significant markers found for cardiovascular mortality and sudden cardiac death (Acharya et al., 2006). Resting HRV has in several studies been linked to the capability to control autonomic responses (e.g., Butler et al., 2006; Park, Vasey, Bavel, & Thayer, 2014).

It is important to note that HRV is not to be confused with HR, which is measured in beats per minute without consideration for the time variation between beats. To get a deeper understanding of the mechanism behind- and surrounding HRV, an explanation of cardiac physiology will be presented subsequently.

Cardiac Physiology

The human heart is a muscular pump with two primary functions. 1) To collect blood poor in oxygen for release in the lungs in exchange for oxygen and 2) to collect and pump the oxygen-rich blood from the lungs to all other tissues in the body. The blood does not only serve the tissues with oxygen but also with other important substances, nutrients, and hormones as well as assisting in removing waste materials. For the blood to circulate, the heart contracts repeatedly through a series of electrical impulses (i.e., action potentials) produced by the sinoatrial (SA) node, which serves as the hearts "pacemaker" (Iaizzo, 2009). The rate of action potentials is what determines HR and is influenced by inputs from the autonomic nervous system (ANS) (Hall, 2006).

When the electrical impulses from the SA node pass through the heart, an electrical current spreads to surrounding tissues with a small part reaching the surface of the body. These currents can be recorded by placing ECG electrodes on the skin on both sides of the heart (Hall, 2006). The ECG produces wave patterns that correspond to and reflects certain events in the cardiac cycle (i.e., the events occurring in the heart during one heartbeat). An example is the QRS complex, which is composed of three waves: Q wave, R wave, and S wave, reflecting the depolarization of the hearts ventricles. The time between two consecutive heartbeats is called the RR interval and equals the time between the highest point of two R waves and it is this, the variation in time between successive RR intervals, that characterize HRV (see Figure 1) (Hall, 2006). Further details on HRV will be provided in later parts, and HRV in relation to the ANS will follow.

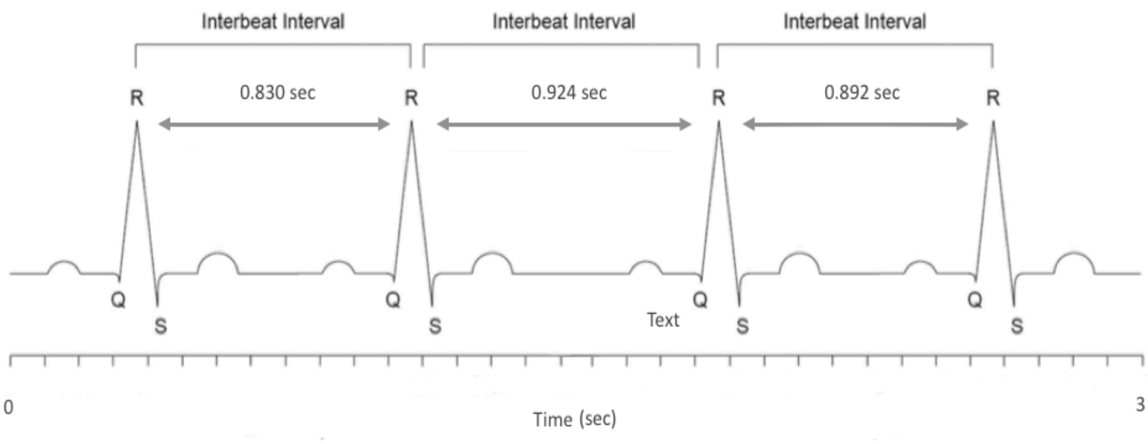

Figure 1. The waveform of four heartbeats. This figure illustrates the characteristics of HRV containing the RR interval between R peaks (inter-beat interval) and the time variation between consecutive heartbeats, as well as some of the characteristics of ECG, including the QRS complex (Inspired by; Appelhans & Luecken, 2006).

Cognitive Neuroscientific Perspective on HRV

Darwin believed that “When an emotional state occurred, the beating of the heart changed instantly, the change in cardiac activity influenced brain activity, and the brainstem structures through the cranial nerves (i.e., vagus) stimulated the heart” (Porges, 1995, p. 302), reflecting his view on how emotion, nervous system, heart, and brain connect. Also the French physiologist Claude Bernard wrote about the intimate connection between the heart and the brain 150 years ago, suggesting a mutual action and reaction mediated by the vagus (Thayer & Lane, 2009). A suggestion supported by e.g. Shaffer and Ginsberg (2017), stating that HRV is an index of neuro-cardiac function, which is generated by interactions between the heart and the brain and dynamic non-linear processes in the ANS. Before further details on associated neural correlates and neural theories, an introduction to HRV and connections with the ANS will follow.

HRV in relation to the ANS. As mentioned, HRV represents the time variation between two R peaks (see Figure 1) (Appelhans & Luecken, 2006). The fluctuations and beat-to-beat variations of a healthy heart are non-linear and complex, even described as a mathematical chaos (Shaffer & Ginsberg, 2017). HRV can be explained as a reflection of the level to which the cardiac activity can meet varying situational demands, i.e. the degree to which the heart and HR respond to the nervous control. Numerous environmental and physiological factors influence HRV although particularly prominent and of importance are the impact of the ANS and the interplay between the parasympathetic and sympathetic branches (Appelhans & Luecken, 2006).

The role of the ANS in governing the performance and behaviour of the cardiovascular system is vast in its complexity and importance (Iaizzo, 2009) as it regulates involuntary bodily functions (Cacioppo, Tassinary, & Berntson, 2007). The branches of the parasympathetic nervous system (PNS) and sympathetic nervous system (SNS) of the ANS typically exert opposing actions (Cacioppo et al., 2007), which allows for essential and swift changes in variables such as HR and contractility (i.e., the ability of the hearts muscle fibers to shorten in response to stimulus). Increased SNS activity, which tends to become dominant during psychological or physical stress, usually causes an excitatory response (such as increased HR) and most commonly decreased HRV, to assist in adapting to various challenges. The PNS activity, on the other hand, tends to increase during relatively safe and stable periods and often results in calming adjustments (such as decreased contractility and HR) and most commonly increased HRV (Iaizzo, 2009). Moreover, the PNS exerts its effects faster (< 1 second) than the SNS (< 5 seconds) (Shaffer & Ginsberg, 2017). How easily an individual can transition between the two states of arousal is hence dependent on the capacity of the ANS to quickly vary HR (Appelhans & Luecken, 2006). It is, however, important to note that both branches of ANS are always active at some level, thus it is rather about which is the most dominant (Robertson, 2004). Furthermore, the relationship between the branches is both linear and non-linear, meaning for example that increase in PSN activity can be linked to non-change, increase or decrease in SNS activity (Billman, Heikki, Sacha, & Trimmel, 2015).

Without the sympathetic and parasympathetic (vagus) influences on HR (more specifically the SA node), the SA node discharge at a rhythmical rate of around 100 times/minute. The alteration from the ANS results in a modification in HR to around 70 beats/minute for a healthy adult. Strong activation of the SNS can increase HR up to 200 beats/minute (excitatory influence on SA node), whereas strong activation of the PNS can result in an HR as low as of 20 beats/minute (inhibitory influence on SA node) (Hall, 2006). Giving evidence to the idea of the heart predominantly being under inhibitory vagal control by parasympathetic influences (Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012). The inhibitory influences are partially controlled by the vagus nerves, which contains about 75% of all nerves in the PNS (Hall, 2006). The effects of the interplaying branches of the ANS are thus producing changes in HRV (Thayer et al., 2012).

As for changes in HR associated with breathing, evidence suggests the variation to be mainly controlled by the vagus nerves (Balzarotti, Biassoni, Colombo, & Ciceri, 2017). The HR increases during inspiration and the RR interval shortens. During expiration the opposite happens, when HR decreases, the RR interval is prolonged. This phenomenon is called respiratory sinus arrhythmia (RSA), which is assessed through observing the respiration-linked variability in HR (Oveis et al., 2009) and is one of the source generating short-term HRV measurements (Shaffer & Ginsberg, 2017). RSA is, moreover, often used as an index of vagal tone (the activity of the vagus nerves, or PNS). According to (Bernardi et al., 2001), breathing can hence be seen as a powerful modulator of HRV. Moreover, RSA and HRV are often used interchangeably, but more specifically RSA is a measure of HF-HRV (given that respiration is controlled for). However, both are believed to reflect variations in cardiac autonomic regulation (Billman, 2011).

Neural correlates of HRV. One important idea about HRV is that it does not only reflect the state of the heart but it also reflects the state of the brain (Thayer et al., 2012). Even though HRV has been studied from a cardiovascular point of view for many decades (and even centuries), it is a relatively new topic within the field of neuroscience. However, over the past several years numerous neuroimaging studies examining brain structures associated with HRV have appeared (Thayer et al., 2012). Several of which are providing convergent evidence; regional cerebral blood flow (rCBF) and task-evoked blood oxygenation level-dependent (BOLD) activity changes in the insula, medial prefrontal cortex (mPFC), amygdala, and anterior cingulate cortex (ACC) have shown to be tightly linked to HRV (Lane et al., 2009; Napadow et al., 2008). These results are consistent with a meta-analysis by (Thayer et al., 2012) based on the data from eight studies ($N = 191$), using positron emission tomography (PET) or fMRI in relation to HRV, specifically looking at cerebral blood flow. Particularly three regions showing significant activation in the overall analysis was found. Two of them located in the mPFC: the right pregenual cingulate and the right subgenual cingulate. The last region showing significant activation was the left sublenticular extended amygdala/ventral striatum (SLEA), a region covering the superior amygdala (central nucleus) and extending into the basolateral amygdalar complex and ventral striatum (Thayer et al., 2012). Moreover, the same meta-analysis tied higher resting HRV to effective functioning of prefrontal-subcortical circuits, which is supporting adaptive and flexible responses to environmental demands (Thayer & Lane, 2009; Thayer et al., 2012).

Additionally, individuals with greater ability to regulate emotions seem to have greater levels of resting HRV (Appelhans & Luecken, 2006). Emotion regulation is believed to depend on the interaction between the amygdala and mPFC, with evidence indicating that the adjacent ACC and the mPFC are involved in down-regulating the amygdala (Etkin, Egner, & Kalisch, 2011). Since the amygdala seems to have neurons with a bias towards encoding negative emotional outcomes (Cunningham, Van Bavel, & Johnsen, 2008) the mPFC appear to be particularly important in the process of evaluating and determining if the threat appraisals are appropriate (Thayer et al., 2012). Furthermore, in studies using rs-fMRI and brain connectivity techniques, additional support was found for the association of HRV with the prefrontal-amygdala pathway (Chang et al., 2013; Sakaki et al., 2016). Greater levels of resting HRV were linked to greater functional connectivity between mPFC and amygdala, possibly demonstrating more efficient communication between mPFC and amygdala in individuals with greater HRV (Sakaki et al., 2016). Nevertheless, it still remains unclear if HRV is associated with the underlying anatomical connections between the PFC and amygdala (Wei, Chen, & Wu, 2018).

Regarding the categorizations and functional boundaries of subdivisions of the PFC (and mPFC), there seems to be little or no consensus. Amodio and Frith (2006) and Bush, Luu, and Posner (2000) have however offered similar explanations for PFC areas linked to HRV, stating they are associated with the physiological features of emotional responses and is according to Thayer et al. (2012) essential in the process of evaluating threat appraisals.

Moreover, to broaden the neuroscientific investigation in relation to HRV an explanation of three theories connected to HRV will follow; the central autonomic network, the neurovisceral integration model, and the polyvagal theory.

The central autonomic network. Many of the neural structures connected to HRV are part of the central autonomic network (CAN), which are believed to be involved in HRV modulation (Beissner, Meissner, Bar, & Napadow, 2013; Benarroch, 1993; Thayer & Lane, 2009; Thayer et al., 2012). CAN have been identified as a unit within the CNS that functionally appears to support adaptability and goal-directed behavior. Functionally it is organized in four interconnected, hierarchal levels: spinal, lower brainstem, upper brainstem, and forebrain. On the first spinal level, the sympathetic and parasympathetic reflexes are influenced by the three other levels (Robertson, 2004). The forebrain regions include several areas of the hypothalamus, which is involved in integrating autonomic and endocrine responses for adaption and homeostasis. It also includes components of the anterior limbic circuit (including insular cortex, anterior cingulate cortex, and amygdala), involved in the integration of goal-related and emotional autonomic responses and bodily sensations. As for the brainstem components these areas are controlling autonomic output and includes the parabrachial nucleus, the periaqueductal gray matter of the midbrain, and several medullary regions. More specifically, the lower brainstem is involved in respiration and reflex control of circulation, whereas the upper brainstem integrates pain modulation with autonomic control and integrated behavioral responses to stressors (Robertson, 2004).

The main output of CAN is mediated through parasympathetic (vagus) and sympathetic neurons innervating the heart. The interplay formed by these inputs to the SA node is the source of the complex variability of the inter-beat intervals. Hence, the beat-to-beat variation (HRV) is directly linked to the output of the CAN. Moreover, sensory information of organs such as the heart (i.e., peripheral end organs) is fed back to the CAN. HRV can thus be seen as an index of CNS-ANS integration and central-peripheral neural feedback (Thayer & Lane, 2000). Important to note is that CAN has been difficult to reveal in humans and is therefore described from animal models (Napadow et al., 2008). The two following theories are partly based on the anatomy of the vagus, which are grounded in the belief of the vagus being influenced by subcortical and cortical regions sub-serving emotion (Sloan et al., 2017), such as regions of the CAN.

Neurovisceral integration model. The neurovisceral integration model, proposed by Thayer and Lane (2000), investigate the direct and indirect connections between the heart and brain. One of the basic ideas of the model being that HRV is more important for what it teaches us about the state of the brain, than the state of the heart (Thayer et al., 2012). The model integrates the attentional, affective and autonomic systems into a structural and functional network, assisting in understanding emotion-regulation and dysregulation. Functionally, the neurovisceral integration model includes, for example, affective information processing, attention regulation, and behavioural and physiological flexibility. Structurally, it includes peripheral end-organs, specifically the cardiovascular system, and central nervous system structures such as the cingulate cortex (Thayer & Lane, 2000).

Thayer and Lane (2000; 2009), and Thayer et al. (2012) propose that there is a central set of neural structures in an organism, which assists in integrating signals from both the inside and outside the body with the purpose to adaptively regulate physiology, perception, cognition, and action. It monitors the external environment and the inner homeostatic processes to enable the generation of adaptive physiological adjustments and motivational drive states. This system is suggested to evaluate the surroundings for signs of threat and safety and then prepare for appropriate action. In essence, the system seems to function as an exceptionally complex "super-system" that integrates activity in motor, interceptive, perceptual and memory systems into a unified representation of a situation and prepare for adaptive responses. Whether or not it is possible for a physiological measure to give indices on the systems ability to provide an adaptive and flexible regulation is not entirely certain. HRV might, however, offer valuable information about the organism's capacity to function in the environment in an effective way and might even provide an easily measured index of the brains integrative system (Thayer & Lane, 2000, 2009; Thayer et al., 2012). The model perceives HRV as the output from the activity of CAN, which remotely regulates the autonomic interplay on the heart. The model suggests that that neural structures of CAN are mutually connected, permitting the prefrontal cortex to use inhibitory control over subcortical regions such as the amygdala, brainstem nuclei, and hypothalamus (Thayer & Lane, 2009).

There are few studies directly addressing this core integration system`s neuroanatomical basis (Thayer et al., 2012). However, in a study by Wei et al. (2018), investigating the anatomical substrates for the neurovisceral integration model, evidence suggests that HRV might actually index an integrative neural network that organizes cognitive, emotional, behavioural and physiological responses in service of adaptability and goal-directed behaviour. The study looked at MRI-based grey-matter volume with a covariance analysis to determine if interregional structural correlations are related to individual HRV- differences. Regarding the amygdala, the findings showed that the covariance patterns encompassed large portions of both cortical and subcortical regions such as prefrontal, insula, cingulate, striatum, hippocampus and midbrain. Providing evidence that the amygdala is of central importance regarding the neural pathways for HRV modulation (Wei et al., 2018). In sum, the theory describes a mutual inhibitory circuit linked to self-regulation processes, where subcortical structures linked to defensiveness such as the amygdala, are under tonic inhibitory control by regions in PFC. The theory stresses the importance of inhibitory neural circuits for flexible and goal-directed behaviour to environmental demands (Balzarotti et al., 2017).

The polyvagal theory. The polyvagal theory introduced by Porges (1995) relates the autonomic function to behaviour. More specifically the theory provides a description of how the paths of the vagus regulate HR (and other visceral organs such as lungs and digestive tract) in response to a variety of stressors and novelties (Porges, 1995). The polyvagal theory proposes two distinct vagal branches, an older unmyelinated and a newer myelinated, with three stages or subsystems that evolutionary emerged, each associated with a unique adaptive behavioural strategy (Porges, 2001).

The myelinated vagus underpins HRV changes (and more approach-related behaviours) and is the first subsystem, which can foster engagement and disengagement with the surroundings by rapidly regulate cardiac output. The unmyelinated vagus supports during threatening or dangerous events through a subsystem associated with immobilization behaviours by reducing metabolic behaviour, while the last subsystem can inhibit the vagus and promote behaviours required for fight or flight (Porges, 2001), and is characterized by the SNS (Kemp & Quintana, 2013).

Moreover, the theory draws on the principle that higher neural circuits inhibit lower neural circuits and that the lower circuits rise in activity when the function of the higher circuits are poorer (Porges, 2007). According to this theory, if an individual perceives threat there are vagal with-drawl (i.e., decreased HRV) and an increase in amygdala activation, triggering fight or flight responses and leading to social with-drawl (Porges, 2011 in Kemp & Quintana, 2013). It is further assumed that the only way social engagement can occur is when there is a perception of the environment as safe, and defence circuits are inhibited (Kemp & Quintana, 2013), or when there is cortical inhibition of the amygdala and increased vagal tone (increased HRV) (Porges, 2011 in Kemp & Quintana, 2013). Arguing that greater HRV (or vagal tone) can be used to index adaptive emotional regulation to the social environment, and may be associated with equanimity, calmness, and lack of distress (Porges, 2007).

The vagus is neuroanatomically connected to cranial nerves regulating social engagement via facial expression and vocalization (Porges, 2001), and originates in several different areas of the brainstem and consists of a family of neural pathways and several branches. There are fibers originating in both the left and right side of the brainstem, where the different sides perform different tasks. Furthermore, the vagus consists of at least 80% afferent vagal fibres and is not merely an efferent pathway (Porges, 1995).

Measurements of HRV

There are various techniques developed to quantify and measure the beat-to-beat variation (i.e., HRV) with the purpose of providing indicators of cardiac autonomic regulation

(Berntson et al., 1997; Malik et al., 1996; Thayer et al., 2012). The different methods to assess HRV are categorized as: spectral- or frequency-domain, time-domain, geometric and nonlinear. Heart rate turbulence and baroreflex sensitivity are two others that can be considered as HRV measures (Kleiger et al., 2005). The starting point for these measures is a simple recording of the time sequence intervals between the heartbeats (the NN interval) of the individual, which usually is extracted from an ECG recording (Martinez et al., 2017). The most common settings where HRV is assessed are either under controlled laboratory conditions using short-term measures of ~5 min for maneuverers used to challenge the ANS, such as drugs or controlled ventilation. Or through 24 hours long-term ECG recordings while the subjects perform their daily activities. The long-term recording is especially useful for quantifying ANS dysfunction and for risk stratifications in several pathological entities and often exemplifies the "golden standard" with greater predictive power in comparison with short-term measures (Kleiger et al., 2005). It is important to report the length of the recording since it greatly effects both time and frequency domain values (McCraty & Shaffer, 2015), and since long and short-term values cannot be used interchangeably (Shaffer & Ginsberg, 2017).

However, there are other ways than ECG to use when measuring HRV. The other method generally applied in clinical environment is photoplethysmography (PPG). Both methods need direct contact with the individual (Kranjec, Begus, Gersak, & Drnovsek, 2014), but when comparing the two PPG is less accurate due to wider signal peaks, possibly affecting the HRV analysis. Additionally, PPG is particularly vulnerable to artifacts (e.g., spurious or missed beats) from motion, thus less reliable in long-term recordings (For review; Kranjec et al., 2014; (Lu & Yang, 2009).

Furthermore, there is a potential for incorrect conclusions since the meaning and significance of the different measures are more complex than often considered. For this reason, a task force by the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, was formed. The goals of the task force were broadly to develop appropriate standards of measurements and terms, as well as to define pathophysiological and physiological correlates, and appropriate clinical applications of HRV (Malik et al., 1996). However, according to Malik (in Martinez et al., 2017), further standardization is needed to get more researchers to use the same technical settings and hence get more mutually comparable measurements available for critical scientific review. Consequently, the possibility of consensus would then be greater regarding the clinical interpretation and correct physiology of these advanced technologies (Martinez et al., 2017).

However, the two approaches primarily used for HRV analysis are frequency or spectral domain and time domain methods (Berntson et al., 1997; Billman, 2011; Malik et al., 1996). The time domain is considered easier to calculate and perform but seem to offer less detailed information in comparison with the frequency domain (Billman, 2011). Because of the limited scope of this thesis and the complexity of HRV measures this thesis will only consider ECG recordings and time or frequency analysis methods, based on recommendations from the task force (Malik et al., 1996). An explanation of the time and frequency methods will follow. However, only methods used in the central studies later presented will be explained.

Time-domain methods. In the time-domain measures, the intervals between the normal QRS complexes, or the instantaneous heart rate (calculated on beat-to-beat basis), are identified. When using an ECG recording, each RR interval are detected and the normal-to-normal (NN) intervals are determined (Malik et al., 1996). The NN interval only includes beats that result from the depolarization originating from the SA node (i.e., the normal electrical activation pattern) and exclude any abnormal beats resulting from, for example, ventricular arrhythmias (i.e., abnormal rapid heart rhythms in the lower chambers of the heart).

The time-domain methods reveal overall ANS modulation. Simple variables can be calculated such as mean heart rate, NN interval and the NN range (longest minus the shortest NN interval) and difference between day and night HRV (Kleiger, Miller, Bigger, & Moss, 1987). There are, however, numerous different time-domain variables, although there are some specific recommended by the task force. For instance the most common measures of NN interval difference; rMSSD (the root mean square of successive difference) NN50 (pairs of bordering NN intervals in an entire recording that differs by more than 50 ms) and pNN50 (NN50 divided by the total amount of NN intervals) (Malik et al., 1996). The latter are only one member of the pNNxx statistic family consisting of both higher thresholds (up to pNN200) or lower thresholds (down to pNN05) (Mietus, Peng, Henry, Goldsmith, & Goldberger, 2002). All three interval difference measures (i.e. rMSSD, pNN50 and NN50) seem to quantify parasympathetic modulation of NN-intervals (Kleiger et al., 2005). Moreover, the different thresholds of pNNxx are proposed to reflect different aspects of HRV, and different aspects of subjective experiences (Trimmel, 2015).

Frequency-domain methods. Frequency-domain or spectral methods represents a unique tool more precise assessment of ANS function (Acharya et al., 2006). The frequency-domain analysis is used to distinguish the waveforms of HRV into the separate component of the rhythms functioning in different frequency ranges. Offering information about the distribution of power (e.g. the amplitude and variance) as a function of frequency (time period) of a rhythm (Mccraty & Shaffer, 2015). The spectrum of these recordings is divided into four components consisting of ultra-low-frequency (ULF) from ≤.003 Hz, very low frequency (VLF) ranging from .003-.04 Hz, low frequency (LF) ranging from .04- .15 Hz, and high frequency (HF) ranging from .15-.4 Hz (Malik et al., 1996). The *total power* is the entirety of the energy in all bands (ULF, VLF, LF, and HF) in 24 hour recordings, and of VLF, LF and HF in short-term recordings or around 5 minutes (Shaffer & Ginsberg, 2017).

The HF component mainly represents parasympathetic activation and is affected by vagal stimulation (Malik et al., 1996). This component is also called respiratory band (Shaffer & Ginsberg, 2017), and is highly influenced by the respiratory pattern. It is, therefore, crucial to control for breathing to improve the findings and reproducibility (Acharya et al., 2006). The interpretation of LF is however widely debated where for example (Malliani, Pagani, Lombardi, & Cerutti, 1991) argue that LF mainly is a marker of sympathetic activity whereas according to (Berntson et al., 1997) the majority of researchers argue that both autonomic branches influence LF HRV. The use of LF/HF as an indicator of autonomic balance is hence not accurate (Billman, 2011), a notion supported by the international guidelines from the task force (Malik et al., 1996). There is, hence, no HRV variables reflecting direct SNS activation (Cygankiewicz & Zareba, 2013). Moreover, according to Porges (2007) there are innate problems with using HF/LF frequencies to quantify HRV if not the neurophysiological mechanisms are understood and dependent factors such as age and context are taken into consideration. As for the VLF and ULF components, it appears to have a stronger association than LF and HF with all-cause mortality (e.g. Tsuji et al., 1996). There is, however, uncertainty concerning the physiological activity influencing VLF and ULF (Kleiger et al., 2005). The most commonly used frequency-domain methods to separate HRV into its components are autoregressive (AR) and the fast Fourier transform (FFT) technique (Berntson et al., 1997). Furthermore, recommended minimum periods of measurements are 24 hour for ULF, 2 minutes for LF, and 1 minutes for HF, and generally, 5 minutes to 24 hours is preferred (Shaffer & Ginsberg, 2017). Moreover, when measuring over an entire 24 hour period there are strong correlations between many time and frequency-domain variables. For example, pNNxx, pNN50, NN50, and RMSSD correlates with HF-HRV.

Dependent factors. There are various factors that may influence the HRV measures, since the cardiovascular system is very reactive to the influence of external stimuli (Bernardi et al., 2001). Gender and age are two major determinants. This is observed as a decline in most frequency and time-domain variables throughout the lifespan, with different patterns of decrease for different variables. The greatest decrease is seen between the second and third decade, and is assumed to be linked to age-decreased parasympathetic activity (Antelmi et al., 2004). Regarding gender, the significant gender-related difference seems to decrease with age, possibly suggesting a hormonal influence on the ANS (Bonnemeier et al., 2003). Menopausal status might, therefore, be an important aspect to control for. Additional variables affecting HRV are; smoking, which seem to reduced HRV (Dinas, Koutedakis, & Flouris, 2013), physical activity (Billman, Cagnoli, et al., 2015), various drugs, including coffee, and invasive procedures (Cygankiewicz & Zareba, 2013), measurement context such as the length of the recording (Shaffer & Ginsberg, 2017), and neurological and psychiatric diseases (Cygankiewicz & Zareba, 2013). Respiration depth and rate are, as mentioned, another potential confound important to consider since it is a powerful modulator of HRV (especially HF) and might, therefore, create potential confounds and error variance (Brown, Beightol, Koh, & Eckberg, 1993). It is well established that the amplitude of HR oscillations gets reduced with increased respiratory frequency and provokes increases in the variability of the RR interval. Contrariwise, HRV increase with reduction in respiratory frequency (e.g., Brown et al., 1993; Hirsch & Bishop, 1981). Additionally, HRV is very sensitive to artifacts, which can significantly distort both frequency and time-domain measures since they increase power through all frequencies (Peltola, 2012). If present, the artifacts of the affected RR-interval can, however, be manually edited out or replaced (Shaffer & Ginsberg, 2017). Lastly, greater HRV can be produced by pathological conditions and is not always healthier (Stein, Domitrovich, Hui, Rautaharju, & Gottdiener, 2005).

The following section will introduce studies examining SWB using HRV measures. The studies will be presented in a falling order, by starting with studies closest to the theoretical framework of HRV and SWB presented above, and end with studies relevant but not fully conforming to the framework.

Measures of SWB with HRV

Subtle characteristics of the variation in HRV conceal information of the underlying mechanisms of HR control, and hence also about the individuals health status (Martinez et al., 2017). As stated, research of HRV in regard of cardiac autonomic changes is a widely accepted tool. The interest in HF-HRV has however extended from being an index of cardiac vagal regulation to also include health and psychosocial functioning (Sloan et al., 2017). However, it is still a new subject with relatively few published studies. A search the 5th of May 2018 on PubMed for “Heart rate variability + subjective well being” generated 241 articles and when adding “measure” only 23 articles were found.

HRV has for instance been measured together with self-reports on SWB. In a recent correlational study, Sloan et al. (2017) examined the relationship between, inter alia, aspects of SWB and HF-HRV. The participants (N = 967; middle to older aged adults) were measured at rest by an ECG recording during 11 minutes, and HF-HRV was calculated using a Fourier transform technique. At a later occasion, SWB questionnaires were completed. The measure used for assessing SWB was (PANAS; Watson et al., 1988), and a self-administered SWB questionnaire consisting of NA (including items such as sad, nervous and hopeless) and PA (including items such as calm, cheerful and full of life), and indices of satisfaction with life, happiness and gratitude. Results revealed that NA was significantly and inversely related to HF-HRV when adjusting covariates including; age, sex, BMI, menstrual status, site, medications affecting parasympathetic activity negatively or positively, smoking, any heart trouble, Parkinson’s or any other neurological condition, history of stroke, and further correlated for respiration rate. However, no significant associations between HF-HRV and any of the other indices of SWB were found.

Others have, however, found associations between HRV and indices of SWB. For example, Schwerdtfeger, Friedrich-mai, and Gerteis (2015) investigated associations between exhibited PA during the day and HRV during the night. The study used an EMA approach to collect participants (*N* = 63; 32 females; mean age 28.84 years) NA and PA-ratings during one day (15 assessments per person). The 9 PA and 6 NA items were divided into activated (e.g. delighted) and deactivated adjectives (e.g. calm). The results were further correlated with the time domain variable rMSSD, recorded by ECG the following night. Bodily movements during the night were controlled for via accelereosensors, as well as age, smoking status, sex, and regular physical activity. A significant positive correlation was found between deactivated PA (e.g., calm) and HRV. No significant association was however found to activated PA, or between HRV and NA.

Moreover, in a study of Chinese students (*N* = 77; 61 females; mean age 20.0 years) conducted by Wang, Lü, and Qin, (2013) that measured affective data (using PANAS) in relation to RSA (estimated by HF-HRV), which were calculated over average 5-min. The RSA was assessed by ECG during a baseline period of 10 minutes, recorded together with respiration data. PANAS was first assessed before the ECG recording and then 4 months and 12 months after the session. The results showed a stable association between trait PA and resting RSA at baseline at all three occasions (r = .54 to .69, p < .001), independent of trait NA, which did not show any significant association to RSA. It was made sure no drugs (nicotine and caffeine included) was taken 2 hours before measures, and that participants had slept well. Findings' indicating that trait positive affect is associated with baseline vagal tone.

Similar results were found in a study by Oveis et al. (2009), where undergraduate students (*N* = 80; 60 females; mean age 20.0 years) participated in a 8-month multiassessment study investigating resting RSA (a measure of HF-HRV) in relation to individual PA and NA at the tonic level. An ECG recording was sampled in a laboratory setting, and RSA assessed for 90 sec and further corrected for artifacts. Following the RSA assessment, the participants viewed slides representing compassion, awe, pride and neutral, after which they rated their positive and negative emotions on an 8-point scale ranging from *not at all* to *strongest possible.* Furthermore, 1 and 6-8 months after the laboratory visit; the participants completed a version of the PANAS evaluating the last months experienced mood. The results showed that resting RSA was significantly positively correlated with PANAS, both for 1 month: $r = .36$, $p < .01$, and 6–8 months; $r = .34$, $p < .05$. No significant correlation was found for negative moods at either 1 or 6-8 months. As for the current emotional responses in relation to the slides, resting RSA was positively connected to positive emotions as a reaction of the neutral slide. No significant correlation was however found between resting RSA and emotional reactions on the slides representing awe, compassion and pride, i.e. the emotion-inducing pictures.

Additionally, a European study ($N = 60$; 18 females; mean age 26.8 years) by Trimmel (2015) discovered correlations between HRV and subjective qualities of affect and good mood. Results were assessed from ECG recordings of 24-hours, by correlating pnXX-variables (ranging from pNN05 to pNN200) as well as frequency-variables (ULF-HF) with subjective experiences such as trait moods (measured by TRIM-T). The findings showed that regarding good mood, all frequency-domain variables were positively, and relatively highly correlated (ULF $r = .37$, VLF $r = .34$, LF $r = .32$, HF $r = .29$), and the strongest correlation from the time-domain variables was with high pNNxx, particularly pNN100 to pNN175 ($r = .36$ to $r = .37$), at a confidence interval of 95%. Indicating that high pNNxx variables are related to PA. The authors further state that in general greater HRV was highly associated with PA. Moreover, an inverse correlation was found between HRV in general and NA (e.g., stress).

Discussion

The aim of this thesis has been to investigate the existing cognitive neuroscience literature on HRV and SWB, respectively. In particular, I have reviewed whether HRV is a reliable method for the objective measurement of SWB.

Due to conflicting evidence and the research still being in its infancy, it is difficult to draw a definitive conclusion on whether HRV is a reliable measure of SWB. The predominant part of the investigated studies did demonstrate a connection between HRV and aspects of SWB (Oveis et al., 2009; Schwerdtfeger et al., 2015; Trimmel, 2015; Wang et al., 2013). Many of these studies did, however, not control for a range of eventual confounders influencing HRV and consists of relatively small sample sizes (N <100). In the only study matching the theoretical framework where the majority of potential confounders were controlled for, with a large nationally representative sample, no correlation between HRV and SWB was found, part from an inverse association with NA (Sloan et al., 2017). Results that are implying that HRV might not serve as a reliable and valid measure of SWB, but might speculatively be able to detect certain aspects of SWB such as deactivated PA (Schwerdtfeger et al., 2015), or indicate inverse associations with NA (Sloan et al., 2017).

As mentioned, the predominant part of the reviewed studies did find associations between HRV and SWB, in particular regarding the affective component. Associations have been found between baseline/resting RSA (baseline vagal tone) and trait PA or positive emotionality, but not trait NA (Oveis et al., 2009; Wang et al., 2013). These results propose that baseline vagal tone may be a stable biological trait of people with a positive emotional style, serving as a help to adaptively react to the surroundings. The results are further in line with psychopathology-studies proposing a positive association between PA and resting RSA, since depression (e.g. lack of PA) often is marked by lower resting RSA (for review; Rottenberg et al., 2002). However, most studies mentioned (Oveis et al., 2009; Sloan et al., 2017; Wang et al., 2013) are only analyzing the HF band and are leaving out remaining variables. Probably due to that the HF are the only variables demonstrating converging evidence of links to physiological mechanisms (i.e., vagal activation) (Trimmel, 2015). One study investigating both all frequency domain variables and the pNNxx family found a positive correlation for all frequency domain variables (Trimmel, 2015), further confusing matter. Regarding the pNNxx variable, it is difficult to interpret since it is unclear exactly what the variable represents. Even though it has been proposed that low pNNxx variables represent NA, and high pNNxx represents PA (Trimmel, 2015), more research is needed to confirm this. However, a great limitation concerning these studies is the lack of control for possible confounding variables such as age, sex, and respiration variables. Where respiration seems to be especially important to control for when using RSA (HF-HRV) as an indicator of vagal tone (Berntson et al., 1997).

As for studies with greater control for possible confounding variables, additional aspects of SWB associated with HRV were observed when distinguishing between activated PA (i.e., feeling activated, dynamic, enthusiastic) and deactivated PA (i.e., feeling calm, relaxed) (Schwerdtfeger et al., 2015). The findings demonstrated a positive correlation between HRV (rMSSD) and deactivated PA, but not activated PA. Results that can be linked to studies showing that activated PA seems to be positively related to physiological activation and sympathetic activity. For instance, excitement has been associated with the same cardiovascular changes as negative emotions, but not to the same extent. This in contrast to deactivated PA which appears to have a stronger association with a number of beneficial physiological variables (for review see; Pressman & Cohen, 2005). For instance, vagal withdrawal has been observed to occur with more activated PA, but not with more deactivated

PA (Čatipović-Veselica et al., 1999). Suggesting that deactivated PA is related to vagal activity. As for the PA items in previously mentioned studies (Oveis et al., 2009; Sloan et al., 2017; Trimmel, 2015; Wang et al., 2013) they either consisted of activated PA (PANAS), unspecified PA items or a mixture of activated or deactivated PA.

In sum, activated PA seems to be related to SNS activity and physiological stress mechanisms, whereas deactivated PA seems to be related to more beneficial physiological variables, and PNS activity. The activation degree of PA might, hence, be linked to different influences on the ANS and HRV (Pressman & Cohen, 2005). It can be speculated that HRV is associated with deactivated PA and not activated PA, since HRV cannot directly assess SNS activity, but rather serve as an index of vagal tone or parasympathetic activation. One can further speculate that when assessing PA through self-reports, the results will turn out differently, partly depending on the composition of activated or deactivated PA items in the particular scale. Further support for this can be interpreted from the polyvagal theory (Porges, 2007), stating that greater HRV (or vagal tone) may be associated with equanimity and calmness, i.e. deactivated PA. However, HRV was assessed during the night in the study by Schwerdtfeger et al. (2015), a factor that may have influenced the results (Acharya et al., 2006). Nevertheless, it was conducted using long-term ECG recording, often exemplified as the “golden standard” with greater predictive power than short-term recordings (Kleiger et al., 2005).

Moreover, the findings of Sloan et al. (2017), displaying an inverse association with NA, can be connected to neuroscientific discoveries and assumptions of the neurovisceral integration model; showing that greater HRV is linked to higher connectivity between mPFC and amygdala, two areas involved in emotion regulation and flexible responses to environmental demands (Thayer et al., 2012). MPFC is believed to evaluate and determine appropriate threat appraisals, and assist in down-regulating the amygdala’s bias towards encoding negative emotional outcomes. Also ACC seems to be involved in the down-regulation of the amygdala (Appelhans & Luecken, 2006). On these bases, it is plausible that greater HRV is inversely linked to NA: where mPFC and ACC can down-regulate the amygdala's negative bias, which may reduce NA. This can also be interpreted as being in line with the polyvagal theory, proposing that greater HRV (increased vagal tone) occur when defense circuits are inhibited, i.e., when there is cortical inhibition of the amygdala. It should, however, be noted that this is only speculative proposals.

Additionally, several studies have shown associations between individuals with greater resting HRV and the ability to regulate emotions (Kemp & Quintana, 2013; Lane et al., 2009). Areas of PFC, ACC, and amygdala are, moreover, associated with CAN. The output of CAN is mediated through vagal neurons innervating the heart, which is directly linked to HRV. Findings that strengthen the connection between mentioned brain-areas and HRV and, hence, the results demonstrated by Sloan et al. (2017). Moreover, since PANAS (consisting of activated PA) served as the measure of PA, the speculation of HRV serving as a measure of deactivated and not activated PA fits with the results from this study as well. However, one limitation of this study is the time lag between measures of SWB and the HRV-data (846 days on average), which possibly might have affected the results. This is however unlikely, according to the authors, since the time lag was controlled for in a supplementary analysis which found to moderating effect on the relationship (Sloan et al., 2017).

Moreover, none of the cognitive measures of SWB showed any association with HRV, indicating that HRV may not be able to index cognitive aspects of SWB, but possibly some affective aspect. Giving further support to the notion that the affective and cognitive aspects of SWB have distinct associations with other variables and should be assessed individually.

Important to note is that the research of HRV and SWB is extremely sprawling, with results and evidence showing inconsistency throughout studies, without any scientific reviews of the connection between the two. Moreover, the subject of HRV is complex with various methods and variables and, to my knowledge, few or no reliable overviews over the meaning and connections of these. There are also many similar concepts that are being used interchangeably, such as RSA, vagal tone, and HRV, which further complicate matter. The lack of common standards regarding measures, analysis methods, used settings, implementation details, and values of different variables, makes the results difficult to compare and comprehend, and generalizations even more challenging.

This problem regarding lack of comparable results between studies may be rooted in, inter alia, the various dependent factors earlier mentioned that may influence HRV, due to the cardiovascular systems sensitivity of external influences (Bernardi et al., 2001). Factors that are well known to be major influences on the results of the measures, such as, age, gender, artifacts, and respiration, are only considered in two of the four studies, clearly demonstrating the need for standardized controls for these potential confounding variables. When these factors are not taken into consideration they have a great risk of disturbing the fallout.

Limitations and Future Suggestions

The greatest limitation of this thesis has been regarding the extremely scares amount of studies investigating HRV and aspects of SWB using similar measurement methods, making it difficult compare the results. Hence, the choice to limit the methods used to ECG and time or frequency domain analysis, and to measure aspects of SWB, due to the greater existing consensus of the construct. Further, the restriction to only present studies measuring SWB and ECG can also be seen as a limitation. Partly due to the very limited selection of studies, and partly since HRV might be able to measure other aspects of WB, for instance, psychological WB. There are, moreover, other studies using other recordings than ECG, which would broaden the number of available studies. It would, furthermore, be interesting to conduct studies with other research designs; since a great part of conducted studies are correlational, and also to analyze additional both time and frequency domains. Another thought for future research is to investigate different aspects of SWB separately, such as the association between activated/deactivated PA and HRV. It is moreover of essential importance that agreements concerning measurements and standardizations of different variables and methods are organized, with larger sample sizes where the possible confounding variables mentioned above are adjusted and controlled for, to be able to get reliable and comparable results and advance the research further.

Conclusion

The apparent importance of the construct of SWB calls for a reliable and valid way to measure it. HRV was chosen as a possible measure since it has gone from just being an index of cardiac vagal regulation to being proposed to relate to WB and emotion regulation (Sloan et al., 2017). When combining the findings, and with eventual confounding variables in mind, it can be speculated that HRV might serve as a measure of certain deactivated aspects of SWB, but may not be able to index the activated aspects of PA. This since HRV cannot directly assess SNS activity, which seems be more tightly linked to activated PA. HRV rather serve as an index of vagal tone, which is more tightly linked to deactivated PA. Results also suggest that HRV can inversely index NA. Support for this claim can be found in the neurovisceral integration model, stating that greater HRV is linked to higher connectivity between mPFC and amygdala; where mPFC can down-regulate the amygdala's negative bias, which may reduce NA. In sum, results from studies with poorer methodological standards demonstrate positive associations between HRV and general PA but not with any cognitive aspects of SWB. In contrast to studies with higher methodological quality demonstrating correlations with HRV and deactivated PA, and inverse associations with NA.

However, it is too early to answer if HRV can serve as a reliable measure of SWB in this initial stage of research. Further standardizations, methodological controls, and studyreplications are needed to assess comparable and reliable results. With more studies of higher methodological quality, the usage and future of HRV as a measure to assess aspect of SWB and other psychological functions are, in my opinion, bright and brimming with likely discoveries. With greater future consensus, HRV could serve well in assessing, for instance, aspects of wellbeing for larger populations and could be used to reach a wider audience due to it being inexpensive, non-invasive, and easy to perform.

In line with Darwin's belief on how our hearts, brains, nervous system and emotions connect, the conclusion can be drawn that it certainly is a complex, interconnected system with many future possibilities for research to investigate.

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