Graduate thesis

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Norwegian University of Science and Technology
Faculty of Social and Educational Sciences
Department of Psychology

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Foreword

The work on this thesis started in the spring of 2017, when professor Patrick Vogel announced that he had acquired innovative technology that allowed for ambulant ultra-short-term measurement of heart rate variability (HRV). Vagally mediated HRV had within the RDoC domain been proposed as a potential biomarker for use in clinical psychology, which could have valuable implications for a renewed diagnostic system and for the evaluation of therapy effects. No one had studied the relation of vagally mediated HRV (vmHRV) to resilience, metacognitions and symptoms of depression and anxiety with this equipment in a large sample before. Based on this, the research questions for my graduate thesis were formulated together with my supervisors. The data from sample one was collected by professor Vogel. The data from sample two was collected by me, with valuable help from Eivind Rauø Strand, Astrid Sødahl, Silje Wiik Sæther, Ingunn Harsvik Ødegaard, Erika Sletten Hanisch and Solveig Løken. The data collection turned out to be time- and effort-consuming, so I am very thankful for the help I achieved on the job. I am also especially grateful for the help and support I achieved from professor Vogel in this phase. He was, together with my supervisors, a key factor in the development of interesting research questions for my thesis. Further, he has continually shared central research findings on the field with me and contributed with technical equipment and necessary financial support for the data collection. The questionnaire was designed by me and I also conducted the analyses. I have received excellent supervision from associate professor Stian Solem and professor Odin Hjemdal, which has been especially valuable in interpreting and writing up the research findings. Senior advisor Kyrre Svarva was also indispensable in the development of the questionnaire. The data set collected consists of several factors that are not included in the current thesis, and it is therefore possible that it will be used in additional research projects. The work on this thesis has turned out to be one of the most demanding, but also one of the most informative processes I have been through in the course of my education. I have learned a lot about the process of conducting psychological basic research from beginning to end, and about the theoretical fields involved in the analyses. Simultaneously, I have learned a lot on the personal level about the pros and cons of juggling many aspirations at the same time. In this relation, I must emphasise the steadfast and priceless support I have received from my husband Eivind, which has been the single most important factor in finishing up this task. Thank you!

Abstract

Introduction: Vagally mediated heart rate variability (vmHRV) has been proposed as a psychophysiological index of self-regulatory capacity and has been found to be significantly lower in individuals with anxiety and depression compared to healthy controls. The main aim of the current study was to investigate the relation between vmHRV, symptoms of anxiety and depression, psychopathology vulnerability factors- (metacognitions) and protective mental health factors (resilience), as well as sleep and physical activity in a large sample of students.

Method: Novel methods in HRV-measurement were employed, in addition to self-reported survey data. The relations between vmHRV, anxiety, depression, metacognitions, resilience, sleep, and physical activity were analysed with correlation- and path analyses.

Results: In contrast to expectations, vmHRV was not significantly correlated with symptoms of anxiety and depression, resilience, metacognitions or sleep quality in the current study. However, vmHRV was weakly correlated in the expected direction to self-reported general physical activity level, which in turn was correlated with symptoms of anxiety and depression, suggesting indirect relationships between vmHRV and symptoms of anxiety and depression. The path analysis showed that resilience in particular appeared to function as a bridge between the physical and mental health factors included in the study.

Conclusion: The study demonstrated that vmHRV can be successfully measured in a large sample in a time-efficient way. The association between vmHRV, physical- and psychological variables in the current study showed complex relationships, suggesting a dynamic interplay between different levels of physiological and mental health factors. Future studies could try to replicate the findings using other methods of measuring vmHRV and demonstrate the associations in longitudinal study-designs.

Contents

Initiatives such as the RDoC (Research Domain Criteria), has been established to integrate knowledge gained from the field of biology, genomics, and neuroscience, to the field of psychology to better understand basic dimensions of mental health (Insel et al., 2010). A central tenet of this framework has been to identify or develop biomarkers that correlate with specified psychological symptoms and to integrate this information to better understand sustaining mechanisms in psychopathology or self-regulation. Despite progress within the field of neuroscience regarding knowledge of brain function, this knowledge has proven difficult to translate into significant new understandings of how to treat, understand, and prevent mental illness (Hajcak & Patrick, 2015). Accordingly, there is still a need for new methods to study and reveal psychophysiological associations in psychopathology.

Heart rate variability (HRV) has been proposed as a psychophysiological index of self-regulatory capacity (Thayer, Hansen, & Johnsen, 2010) and possibly a useful biomarker for analysis in the RDoC matrix (Hajcak & Patrick, 2015). HRV refers to the beat-to-beat variation in heart rate. It has been considered a proxy of parasympathetic control and vagal tone (Berntson et al., 1997) and is assumed to be an indicator of the regulatory flexibility of the autonomous nervous system in response to changing physiological and psychological states (Appelhans & Luecken, 2006; Zahn et al., 2016). This assumption builds on the theoretical frameworks provided by both the Neurovisceral Integration Model (Thayer & Lane, 2000; Thayer, Hansen, Saus-Rose, & Johnsen, 2009) and the Polyvagal Theory (Porges, 2001, 2007). These theories link HRV to cognitive- and emotional regulation as well as social engagement; qualities that can be understood as indicators of self-regulatory capacity. Both models hypothesise that individual differences in resting state HRV reflect individual variations in the ability to inhibit dominant impulses and behaviours, where higher levels of HRV is theorised to reflect better inhibitory abilities in both automatic and deliberate regulatory processes (Zahn et al., 2016). HRV assessed by measuring the rapid changes in heart rate mediated by the vagus nerve (parasympathetic activity) is referred to as vagally mediated HRV (vmHRV). Vagally mediated HRV is commonly used to study individual differences in resting state HRV and the relationship between these differences to mental and physical health. HRV and vmHRV as terms are often used interchangeably in the literature. The current study will also apply both terms to refer to vagally mediated HRV (also called baseline HRV, resting state HRV, etc.) as the current study only discusses vmHRV.

Vagally mediated HRV has been linked to neural circuits that regulate emotion, cognition and behaviour (Beauchaine & Thayer 2015; Gruber, Mennin, Fields, Purcell &

Murray, 2015) and a growing body of evidence links vmHRV to psychopathology. A meta-analysis based on 36 studies, including 2086 patients with an anxiety disorder and 2294 controls, found anxiety disorders to be associated with reduced vmHRV (Chalmers, Quintana, Abbott, & Kemp, 2014). Across studies, Hedges' *g* (95% CI) for the relationship between time domain vmHRV and all anxiety disorders was -0.45 (-0.57 to -0.33), $p < .001$. This is considered a moderate effect.

Depression has also been linked to vmHRV (Kemp et al., 2010) in a meta-analysis that found that patients with major depressive disorder (MDD) had lower vmHRV compared to healthy controls with a Hedges' *g* of -0.30, $p < .001$. Further, depression severity was weakly, but significantly negatively correlated with HRV ($r = .35$, $p < .001$). Another study by Kemp, Quintana, Felmingham, Matthews and Jelinek (2012) investigated vmHRV in unmedicated physically healthy MDD patients ($n = 73$) compared to healthy controls ($n = 94$) in a case-control study. This study found that vmHRV was reduced in MDD relative to controls, with a $d = -0.48$. The greatest impact on vmHRV was found in MDD patients with comorbid GAD ($n = 24$) relative to controls (Cohen's $d = 0.84$), indicating a large effect size.

Even though the investigation of the relationship of vmHRV to depression and anxiety has yielded significant findings, studies have generally shown small to moderate effect sizes (see e.g. Rottenberg, 2007; Kemp et al., 2010; Chalmers et al., 2014). Several studies have also failed to find significant associations between HRV and symptoms of depression and anxiety. One example is a study by Gehi, Mangano, Pipkin, Browner and Whooley (2005) on 873 outpatients with stable coronary heart disease. Depressive symptoms were assessed using the modified Computerized National Institute of Mental Health Diagnostic Interview Schedule (CDIS-IV) and the 9-item Patient Health Questionnaire (PHQ-9). HRV was assessed in the time- and frequency domain. The researchers found no evidence of an association between depression and HRV. This finding is particularly interesting because it raises questions about the potential role of HRV in the association between depression and cardiovascular disease. An example of a study that failed to find an association between heart rate variability and anxiety symptoms is that of Pitzalis et al. (2001) on patients ($n = 103$) who had survived a myocardial infarction.

Another aspect that is worth noting when reviewing the literature on HRV is methods of measurement. Effect sizes have been shown to vary depending on the method of HRV measurement; e.g. in depression, where non-linear methods have shown large associations compared to time domain and frequency domain measures (Kemp et al., 2010). Also, the research on HRV and mental health is mainly based on small and selected samples, e.g.

subjects fitting the DSM-criteria (Diagnostic and Statistical Manual of Mental Disorders; American Psychiatric Association, 2013) of a mental disorder. As the RDoC framework seeks to look beyond the current diagnostic system to establish a more integrated and thorough understanding of psychopathology, there is a need for larger studies of the general population to establish whether significant intersubjective differences in HRV exist in meaningful relation to differences in psychological and physical functioning. If HRV is an important indicator of mental health we would expect it to be 1) significantly related to symptoms of mental disorders, 2) significantly related to factors such as physical activity and sleep, as they are known to impact on both mental and physical health, and 3) to relate meaningfully to central psychological models on mental health. Two such models are the metacognitive model of psychopathology (Wells, 2009), and the resilience framework (i.e. Southwick, Bonanno, Masten, Panter-Brick & Yehuda, 2014) for mental health.

Maladaptive metacognitions have been found to be implicated across mental disorders (Sun, Zhu, & So, 2017). Sun et al. (2017) conducted a meta-analysis showing elevated maladaptive metacognitions (as measured by the Metacognitions Questionnaire 30 [MCQ-30]; Wells & Cartwright-Hatton, 2004) in patients as a group on all MCQ dimensions, supporting maladaptive metacognition as a transdiagnostic factor across diagnostic groups. No studies have investigated the link between metacognitions and HRV.

HRV has also not been investigated in relation to resilience. Resilience is a term used to highlight that individuals respond differently to stress (e.g. Werner & Smith, 2001), and several individual, family and community level resilience factors have been identified as protective factors between life adversities and mental health (Fritz, de Graaff, Caisley, van Harmelen, & Wilkinson, 2018). HRV has been suggested as a potential marker of self-regulatory capacity in relation to stress. In a study by Fabes and Eisenberg (1997) regulatory control (vagal tone) was found to interact with situational factors in influencing the prediction of stress-related responses in adults. Based on these findings the relationship between HRV and resilience should be investigated further.

Another central factor in mental health is sleep quality. Sleep is often disrupted in patients with depression or anxiety disorders (Sandor & Shapiro, 1994; Ramsawh, Stein, Belik, Jacobi, & Sareen, 2009; Bower, Bylsma, Morris, & Rottenberg, 2010) and there are indications that insomnia generally increases the risk of psychopathology (e.g. Hertenstein et al., 2018). A study on a large randomly selected sample (n = 3000, aged 20-60 years) by Jansson-Fröjmark & Lindblom (2008) found a bidirectional relationship between anxiety and depression on one hand, and insomnia on the other hand, over the course of a year. It was found that future insomnia was related to both anxiety and depression, and that anxiety was the most prominent mechanism in explaining future insomnia. The results also showed that insomnia predicted future depression better than future anxiety. Sleep has also been related to HRV. In a study conducted by Castro-Diehl at al. (2016) individuals (*n* = 527) from a population-based sample followed different sleep patterns based on a sleep protocol and conducted several stress inducing tasks with recovery periods while HRV was measured using EEG at different points of measurement. They found that participants who slept less than 7 hours per night had lower baseline values of high frequency HRV (HF-HRV) than those who slept 7 hours or more per night. They also found that participants with low sleep efficiency had lower baseline values of HF-HRV than those with higher sleep efficiency. Participants who slept less than 7 hours per night further had greater increase in HF-HRV during recovery from mental stress. HRV thus seem to be associated with short sleep duration, low sleep efficiency, and insomnia combined with short sleep duration (Castro-Diehl et al., 2016).

A factor that has been found to improve sleep quality and duration is physical activity. However, beneficial effects have been found to be small-to-medium and moderated e.g. by sex, age, exercise type and baseline physical activity level (Kredlow, Capozzoli, Hearon, Calkins, & Otto, 2015). Physical activity could impact on both physical measures, such as HRV, and mental health, although the underlying mechanisms have not been fully illuminated. Proposed mechanisms have spanned from neurobiological to psychosocial and behavioural (Lubans et al., 2016). Evidence has been established to support the effect of physical activity on mental health in youths via improvements in physical self-perceptions accompanied with enhanced self-esteem (Lubans et al., 2016). Inactivity can further be linked to obesity which has been shown to increase risk of depression in children and adolescents (Quek, Tam, Zhang, & Ho, 2017). Vigorous physical activity, but not moderate activity has further been found to predict higher HRV (LnRMSSD) among younger adults (*n* = 82) after controlling for age, gender, and diastolic blood pressure (May, McBerty, Caky, & Gianotti, 2017).

Based on the literature reviewed, the main aim of the current study was to investigate the relation between the physiological measure vagally mediated heart rate variability (vmHRV), vulnerability- (metacognitions) and protective factors (resilience), sleep and physical activity, as well as symptoms of anxiety and depression. How these factors are associated in a large population of students has to our knowledge not been investigated. Further, the current study utilises a novel method for HRV-assessment (Flatt & Esco, 2013) with a software called ithlete (developed by HRV Fit Ltd.). This method allows for ultra-short-term ambulatory assessment of vmHRV. Thereby, the study links objective physical data to subjective self-reported data on physical and psychological parameters.

The current study set out to investigate the following hypotheses:

Hypotheses

1. A single assessment of resting state vmHRV is expected to be representable for the mean of successive vmHRV assessments within a limited time period of two weeks.
2. vmHRV is expected to correlate significantly and negatively with maladaptive metacognitions, and symptoms of anxiety, depression, and poor sleep quality. Furthermore, vmHRV is expected to correlate significantly and positively with resilience factors and physical activity.
3. Innovative software for ultra-short-term ambulatory assessment of vmHRV is expected to generate values that correspond to results for the same age group in comparable studies that have used other validated HRV assessment methods.

Methods

Participants

Sample one. The participants were Norwegian adults (*n* = 11), ranging from 26 to 68 years. Four were females and seven were males. This sample was included to investigate the stability of the HRV scores measured with the ithlete equipment.

Sample two. In total 217 subjects gave their consent to fill out a questionnaire and measure heart rate variability (HRV). We have HRV-values on 203 participants, due to unstable signal during testing on the remaining 14 participants. The sample used in the analysis consisted of participants with complete measurements on all the included variables, yielding a sample size of 201.

The participants in the selected sample were young Norwegian students, with a mean of 21.6 (2.7) years (range 18-29 years). There were 145 females and 56 males. Mean body mass index (BMI, kg/m^2) was 22.7 (*SD* = 3.6, range 11.4 to 46.5). Eighty four percent were single or in a relationship, but not cohabitants or married. The majority of the subjects reported upper secondary school as highest completed level of education. Approximately 60% of the subjects reported a moderate level of physical activity, and the other 40% were split approximately equally between low and high levels of physical activity. Only two participants reported smoking on a daily or weekly basis and four reported to drink equal to or more than 14 units per week. Seven participants reported taking antidepressants. No participants reported having a cardiovascular disease. However, approximately 40% reported having a physical illness confirmed by a physician, where skin disease, respiratory disease and neurological diseases were the most common. Table 1 in the results section provides a thorough overview of demographic and descriptive data of the sample analysed (*n* = 201).

Procedure

Sample one. The 11 participants were recruited through convenience sampling. They were each given their own ithlete finger sensor and tablet computer with the ithlete app installed. They were instructed to do one measurement a day in a resting state, preferably in the morning before breakfast and in a seated position. The first thirteen days of measurement were used in the analysis.

Sample two.

Inclusion criteria. Inclusion criteria for the study were signed written informed consent and age between 18 and 30 years. It was decided to limit the age to this range in order to control for the variation in HRV through the lifespan (Zulfiqar, Jurivich, Gao, &

Singer, 2010). There were no exclusion criteria. The sampling was driven by the aim to collect representative data for young students in Norway within the age span of 18 to 30 years. Approximately 280 individuals within the current age span were requested to participate in the study through a quick verbal presentation of the study. Out of these, 217 showed up to receive further information about the study in writing. Thus, the response rate was approximately 77.5%. All subjects who received written information about the study and study procedure chose to participate.

Recruitment. Approximately half of the sample (*n* = 96) were students at Folk High Schools. They were recruited at the morning assembly of each of the two schools we visited. A Norwegian Folk High School is a boarding school that students normally attend for one year only, most often after they have graduated from upper secondary school. The schools have a large variety of subjects with a focus on self-development and education for life. They have no entrance exams or final exams. Common course options include outdoor skills, travel skills, sports, land use skills, the arts and music. All students are eligible for financial aid from the state and are therefore not dependent on savings or financial aid from family. This also applies to students attending higher education in Norway.

The other half of the sample (*n* = 103) were university students in the six-year clinical master's degree programme in psychology. They were recruited through their participation in a mandatory subject that occurs on the first through forth semester on the study programme. The remaining participants (*n* = 2) were also university students, but attended other master degree programs. They were recruited through convenience sampling.

VmHRV measurement and questionnaire procedure. The assessment of vmHRV was conducted with the ithlete finger sensor and app (Flatt & Esco, 2013) installed on tablets.

The participants were gathered in classrooms or auditoriums in the Folk High Schools or at the University. Each participant was seated at his/her own desk. Here, they read an information leaflet and signed a consent form approved by the Norwegian Regional Committees for Medical and Health Research Ethics (REC; case number 2017/1212). Then they began to fill out the questionnaire. Meanwhile, we started measuring vmHRV by approaching participants, requesting them to pause filling out the questionnaire while we measured HRV. As soon as the HRV was measured and recorded, the participants could proceed to finish the questionnaire. In all, participation took approximately 25 to 30 minutes when we could successfully record HRV on the first or second trial.

All assistants were given the same instructions on beforehand on how to guide the participants through the HRV measurement procedure. The participants were asked to lay their forearms on the desk, with the inside of their hands facing upwards, and keeping the arms relaxed in this position throughout the procedure. This is to stabilise the signal from the finger sensor (see Allen, 2007 for a topical review of photoplethysmography and its application in clinical physiological measurement). Next, the finger sensor was placed on the index finger of the non-dominant hand. HRV was therefore mostly measured on the participants' left index finger. Esco, Flatt and Nakamura (2017) found high correlations ($r \geq .98$) between the ithlete finger sensor and ECG measurements, and we wanted to be in line with their procedure (they placed the finger sensor on the left hand index finger), as this is one of few studies published using the ithlete finger sensor. However, Esco et al. (2017) do not specify whether they chose the left hand because this was the non-dominant hand of all participants ($n = 30$). We chose to measure the non-dominant hand due to literature suggesting that there might be a statistically significant higher peripheral capillary hemoglobin oxygen saturation (SpO_2) in the dominant hand vs. the non-dominant hand (Basaranoglu et al., 2015).

In a few cases (< 10), where we could not get a signal from the index finger, we placed the sensor on the middle finger or the ring finger. According to Basaranoglu et al. (2015) there are measurable differences in oxygen saturation (SpO_2) between these fingers, but the differences are small and probably not of clinical importance.

At least one minute was allowed for heart rate stabilisation before the recording was initiated, as recommended by Esco et al. (2017). The participants were told to sit calmly and follow the breathing instructions on the application. The application demonstrates the pace in which you should breathe in and out with a moving circular animation on the screen. The application also continuously instructs the user to breathe in through the nose and out through the mouth in this controlled pace. It is known that the respiration cycle affects HRV results and that "free breathing" therefore does not provide a reliable measure of HRV (see e.g. Brown, Beightol, Koh, & Eckberg, 1993; Saboul, Pialoux, & Hautier, 2013). Thus, the controlled breathing facilitated by the app, enable quantitative inter-individual comparisons and improve reproducibility and reliability of test findings. It takes 55 seconds to assess HRV with the ithlete application. In 14 cases we were not able to measure HRV. As a general rule, we stopped trying to measure HRV after three failed trials.

Measures

Patient Health Questionnaire-9 (PHQ-9; Kroenke, Spitzer & Williams, 2001). The PHQ-9 is widely used as a self-report questionnaire in screening, diagnosing, controlling for, and in investigating the level of severity of depression in research. It consists of nine symptom criteria of depression. Criteria items present during the past two weeks are rated on a scale from 0 (not at all) to 3 (almost every day). Scores between 0-4 indicates minimal or no depression, scores of 5-9 mild, 10-14 moderate, 15-19 moderate to severe, and 20-27 severe levels of depressive symptoms (Kroenke, Spitzer, & Williams, 2001). A meta-analysis by Manea, Gilbody and McMillan (2012) found that the PHQ-9 had acceptable diagnostic properties for major depressive disorder for cut-off scores between 8 and 11. The internal consistency has been shown to be good with a Cronbachs alpha of .89 (Kroenke, Spitzer, & Williams, 2001). In the current study the internal consistency for the measure was good (α = .86). In the current study, the total sum score was used in the analysis.

Generalized Anxiety Disorder 7-item Scale (GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006). The GAD-7 has been applied in screening, diagnosing, and controlling for the presence of generalised anxiety in research. It consists of seven symptom-based criteria of generalised anxiety experienced during the last two weeks. Presence of symptoms are ranged on a scale from 0 (not at all) to 3 (almost every day). Scores between 0-4 indicates minimal levels of anxiety symptoms, 5-9 mild, 10-14 moderate, and 15-21 severe levels of anxiety. A suggested cut-off for diagnostic levels of anxiety is a score of 10 or higher (Spitzer et al., 2006; Kroenke et al., 2007). The measurement has shown good internal consistency with a Cronbach alpha of .92 (Spitzer et al., 2006). In the current study, the internal consistency for the measure was good (α = .85). In the current study, the total sum score was used in the analysis.

Resilience Scale for Adults (RSA; Hjemdal, Friborg, Martinussen & Rosenvinge, 2001; Friborg, Hjemdal, Rosenvinge, & Martinussen, 2003). The RSA is a self-report inventory with semantically differentiated response alternatives. It rates six hypothesised protective factors associated with psychological resilience: 1) Perception of self, 2) Planned future, 3) Social competence, 4) Structured style, 5) Family cohesion, 6) Social resources. Higher scores indicate higher levels of resilience. The internal consistency has been shown to be excellent (α = .90; Hjemdal et al., 2001). The internal consistency for the mean score of the measure used in the current study was excellent (α = .90).

Metacognitions Questionnaire-30 (MCQ-30; Wells & Cartwright-Hatton, 2004). The MCQ-30 measures individual differences in metacognitive beliefs about thinking and thinking processes. It consists of 30 items rated on a four-point scale ranging from 1 (do not agree) to 4 (strongly agree). Further the MCQ-30 has five subscales each with a range from 6-24 points: 1) positive beliefs about worry, 2) negative beliefs concerning the uncontrollability and perceived danger associated with worry, 3) cognitive confidence, 4) need to control thoughts, and 5) cognitive self-consciousness. The higher the participant rates each item, the greater dysfunction regarding the item is evaluated. The MCQ-30 has shown excellent internal consistency for the full scale ($\alpha = .93$) and for the subscales (Wells & Cartwright-Hatton, 2004). The internal consistency for the total score used in the current study was good ($\alpha = .88$).

Physical activity. Participants were asked "How would you rate your level of physical activity?" and rate their response on a scale from 1 (very low) to 10 (very high).

Subjective sleep quality. The component "Subjective sleep quality", which is one of seven component scores in the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989; Norwegian version by Franer, Nordhus, Pallesen, & Øverland, see Appendix E) was used in the analysis. This component consists of one question, which is the following: "During the past month, how would you rate your sleep quality overall?" The participant can choose from four different answers: Very good, fairly good, fairly bad, and very bad. These answers are rated on a scale from 0-3, from very good (0) to very bad (3) sleep quality. A standardisation study of the PSQI on three different samples in Norway (Pallesen et al., 2005) found that the component "subjective sleep quality" showed the highest correlation with the total PSQI score (*r* ranging from .56 to .66, depending on the sample) among the seven components. Based on these findings, the current study chose the "subjective sleep quality component" for analyses.

HRV assessment. The gold standard technique when measuring HRV involve recording of ECG-signals from which beat-to-beat cardiac time intervals (RR intervals) are analysed. This procedure can be inconvenient and time consuming when the aim is to investigate intersubjective differences in HRV, as this e.g. requires larger sample sizes. Schäfer and Vagedes (2013) have discussed utilising photoplethysmography (PPG) instead of ECG, as it can simplify ambulatory monitoring of HRV. PPG technology is a simple, non-invasive and low-cost optical technique that detects blood volume changes in the microvascular bed of tissue (Allen, 2007), which can be used to assess pulse rate variability.

Recently, an international software and biosensor development company, HRV Fit Ltd., have developed a finger sensor and app called ithlete that utilises PPG technology to assess time domain vmHRV for an ultra-short time period of 55 seconds. The finger sensor has been scientifically validated by Heathers (2013). He tested the accuracy between ECG and finger sensor assessment (PPG), both at rest and during experimental stress. Heathers (2013) found that the PPG technology records a pulse-to-pulse approximation of an ECG-derived heart rate series that is sufficiently accurate to perform time- and frequency-domain analysis of its variability. Esco et al. (2017) tested if the ithlete equipment could provide an accurate estimate of ultra-short-term vmHRV compared to ECG results. The accuracy was tested in supine, seated and standing positions in 30 healthy and athletic college aged subjects. All positions had correlations of .98 or higher to ECG. The ithlete and ECG LnRMSSD values were non-significantly different in the supine position ($p = .63$), but significantly different in the seated ($p < .01$) and standing ($p < .001$). The effect sizes for the comparisons of the methods in the three positions were however considered to be trivial (Cohen's *d* ranged from 0.01 to 0.15), suggesting that no practical differences exist (Esco et al., 2017). The ithlete app and sensor, which can be used with a tablet, thus constitutes an innovative and practical way of measuring and collecting HRV data in large samples and was therefore employed in the current study.

Ithlete uses a time domain parameter; RMSSD (Root Mean Square of Successive Differences), that correlates very highly with the more complex frequency domain measure HF, without requiring a breathing rate greater than nine breaths per minute or stationarity of underlying heart rate (Flatt & Esco, 2013). The HRV values are presented to users of the ithlete app by the formula LnRMSSD x 20 (Log transformed RMSSD; Flatt & Esco, 2013).

Data analyses

Descriptive statistics for the variables included in analysis was conducted. These are included in Table 1, together with relevant demographics and HRV data.

Assessment of skewness and kurtosis (see Table 2) for the variables included in analysis, showed that the vmHRV data (log transformed RMSSD values), RSA data, physical activity, and sleep quality data were normally distributed. However, the MCQ-30 data were moderately positively skewed (0.71, $SE = 0.17$), the GAD-7 data highly positively skewed (1.02, $SE = 0.17$), and the PHQ-9 data were highly positively skewed (1.53, $SE = 1.53$) and had a little higher kurtosis (2.81, $SE = 0.34$) compared to what is expected for normal distribution. These findings could indicate that the MCQ-30, GAD-7 and PHQ-9 data from the sample are divergent from what we would expect, considering the large sample size. However, these data are as expected, as these three measures are screening tools for maladaptive metacognitive beliefs associated with psychological disorders, for symptoms of anxiety disorders, and symptoms of depression, respectively. Normative data of the GAD-7 and the PHQ-9 (this was not found for the MCQ-30), suggest that the total score distributions are positively (right-) skewed in the general population (Löwe et al., 2008; Tomitaka et al., 2018). To check whether normal distribution of the MCQ-30, GAD-7 and PHQ-9 would make a difference to the results, square root transformation of these variable values was tested. The transformation did not make a difference of significance to the results in the correlational and path analyses, as they only changed at the second decimal level. Thus, the current study did the planned analyses without transformation.

To get an indication of how representative the first measurement with the ithlete app was for consecutive measurements, Cronbach's alpha was calculated based on 13 points of measurement from the 11 participants in sample one. To further explore the representativity of a single measurement for subsequent measurements, a correlation analysis comparing first time HRV measurement and the mean of all 13 measurements for the 11 subjects was executed. Correlational analyses were undertaken to investigate the association between HRV, metacognitions, resilience, sleep and physical activity, to symptoms of anxiety and depression in sample two (see Table 4 for results).

To further investigate the relationships between the measured variables, two path models were specified (see Figure 1 and 2). As no other research on the current specific set of variables has been found, the current study took an exploratory approach in hypothesising the path models. In building the model, one of the central questions was whether to place resilience or metacognitions as the exogenous, independent variable. To the author's knowledge there does not exist an evidence based theoretical framework that integrates both concepts. Thus, both variables could arguably be placed before the other in the model, depending on the perspective. Furthermore, it is important to keep in mind that the cross-sectional design does not allow for conclusion regarding causation. Therefore, an approach based on going from more general to more specific variables was chosen. Resilience is an umbrella term collecting several factors that have shown protective capabilities in the relationship between adverse events and symptoms of anxiety and depression (Fritz et al., 2018). As such it represents a general construct and is not tied to one single theory. The inventory developed by Hjemdal et al. (2001) in the current study was developed based on several domains and factors shown in the literature at that point to be related to resilience. In a similar vein, metacognition as a construct also refers to a variety of factors. However, in the current study the Metacognitions Questionnaire (Wells & Cartwright-Hatton, 2004) measure specific dimensions of dysfunctional metacognitions that are hypothesized and shown through research to be related to symptoms of anxiety and depression. These dysfunctional metacognitions are hypothesised in a specific model of psychopathology (the Self-Regulatory Executive Function model [S-REF]; Wells & Matthews, 1996) to be the main cause in initiating and sustaining emotional disorders. It can therefore be thought of as a specific vulnerability factor in this framework. Therefore, resilience was chosen as the exogenous variable in the path models. This choice was also supported by the correlational findings; compared to maladaptive metacognitions, resilience showed significant associations to more of the other variables included in the study. The directions of the paths for the rest of the variables were based on the correlations found between them and the empirical findings reported in the introduction.

To test the path models specified, the AMOS application for SPSS (Arbuckle, 2014) was employed. AMOS provides several goodness of fit indices of the hypothesised model. The most commonly used statistic test for the assessment of model fit is the chi-square goodness of fit test (χ^2), which estimates the discrepancies between the observed covariance matrices and those indicated by the model. If the chi-square value is non-significant, this indicates adequacy of a model. However, it only assesses the absolute fit of the model to the data, and thus it is impacted by sample size and often inflates type-I error (Cohen, 1988; Bollen, 1989). For this reason, other indices can be applied to evaluate the model fit. According to Hu and Bentler (1999) two types of fit indices should be reported; the standardised root mean square residual (SRMR) and a comparative fit index such as the root mean square error of approximation (RMSEA). The assessment of model fit was done according to Hu and Bentler (1999). RMSEA <.06 and SMRS <.08 represent good fit for the model. Values for the Comparative Fit Index (CFI) and the Tucker-Lewis Index (TLI) are also reported, where values close to .95 are needed (Hu & Bentler, 1999). To test for significance of the indirect effects in the model, bootstrapping was performed based on 500 samples and the confidence interval set to 95%.

To compare the HRV data in the current sample to data from other comparable studies, effect sizes were calculated using Cohen's *d*, based on the means and standard deviations of the current study and three comparable studies (Melanson, 2000; Zhang, 2007; Zulfiquar et al., 2010). Sawilowskys (2009) new effect size rules of thumb, that builds on Cohen (1988), were used when interpreting the results; 0.01 is considered a very small effect, 0.20 a small effect, 0.50 a moderate effect and 0.80 a large effect.

Missing data. In total 201 participants of 217 had HRV measures that could be utilised. For the other measurements there were few incidents of missing data: GAD-7 had 0.5% missing, PHQ-9 had 2.0%, MCQ had 5.0% missing, and RSA had 4.5% missing. Missing items for GAD-7 and PHQ-9 were replaced using mean item scores for the total sample on the respective items. For the RSA and MCQ missing items were replaced with the mean score on the respective subscales.

Results

The mean scores for symptoms of anxiety and depression were within the minimal to mild ranges. However, 26% of the sample scored above 8 on the PHQ-9, which indicates that a large amount of the sample reported clinical levels of depression (Manea, Gilbody and McMillan, 2012). Further, in the current sample 18% reported a score above the suggested cut-off for clinically significant anxiety (Spitzer et al., 2006; Kroenke et al., 2007). Approximately 80% of the sample reported sleeping more than seven hours per night in average the past month, and around 80% rated their sleep quality as fairly or very good. Approximately 60% of the sample reported a general level of physical activity within the moderate to high range. Only two participants reported smoking daily or weekly and the majority of the sample reported low levels of alcohol and drug usage. No participants had cardiovascular diseases. Seven participants reported using antidepressants, two used anxiolytica, and seven sleeping medication regularly. See Table 1 for more demographic and descriptive information on the analysed sample.

Table 1. *Demographic and Descriptive Data of the Analysed Sample*

Variable	*N*	*M*	*SD*	*Range*
VmHRV (LnRMSSD)	201	4.16	0.41	2.95-5.45
Level of physical activity	201	5.53	2.14	1-10
Subjective sleep quality	201	1.01	0.73	0-3
GAD-7	201	5.73	4.27	0-21
PHQ-9	201	5.64	4.71	0-24
RSA	201	5.10	0.78	2.94-6.70
MCQ-30	201	49.84	11.44	30.00-86.00
Sleep duration	200	7.33	1.03	4.00-10.00
		Level	*N*	%
Education	199	Primary and lower secondary school	4	2.0
		Upper secondary school	148	73.6
		University degree, 1-4 years	38	18.9
		University degree, >4 years	9	4.5
Level of physical activity	201	Low (1-3)	39	19.4
		Moderate (4-7)	124	61.6
		High (8-10)	38	18.9
Average sleep duration past month	200	Under 7 hours	41	20.4
		7 to < 8 hours	85	42.1
		≥ 8 hours	74	36.8
Subjective sleep quality past month	201	Very good	45	22.4
		Fairly good	116	57.7
		Fairly bad	33	16.4
		Very bad	7	3.5
Smoking status	195	Daily or weekly	2	1.0
		Does not smoke	183	91.0
Alcohol units usually consumed per week	197	0	66	32.8
		1-6	118	58.8
		7-13	9	4.5
		≥14	4	2.0
Cardiovascular disease, diagnosed by physician	201	Yes	0	.0
Antidepressants	195	Yes	7	3.5
Anxiety inhibitory medication (anxiolytica)	195	Yes	2	1.0
Sleeping medication (hypnotics/sedatives)	195	Yes	7	3.5

Note. n = 201. VmHRV (LnRMSSD) = Vagally mediated heart rate variability (Log transformed root mean square of the successive differences), GAD-7 = Generalized Anxiety Disorder Scale, PHQ-9 = Patient Health Questionnaire, RSA = Resilience Scale for Adults, MCQ-30 = Metacognitions Questionnaire. All variables but vmHRV values are self-reported. Body mass index is calculated from self-reported height and weight. Education = highest level of education at time of participation.

Reliability and correlations of subsequent HRV measurements

The Cronbachs alpha, comparing all first 13 measurements between all 11 subjects in sample one, was excellent (α = .99), indicating high internal consistency between points of measurements. Further, the correlation between the first assessments and the mean of all 13 assessments was high (r = .88, p = .001). Together these two analyses indicate that a single measurement of vmHRV with the ithlete equipment can be applied as a reliable representation of subsequent vmHRV measurements within a limited time period of at least two weeks. Table 2 gives an overview of the first vmHRV assessment values, mean and range of all 13 assessments for the 11 subjects in sample one. The table shows that the first assessments for the 11 subjects generally were close to the mean values for all 13 assessments. The mean standard deviation was .34. This indicates that in average approximately 68% of the data was within ±.34 from the mean value. The ranges show that some larger deviations from the mean occurred. The average difference between the smallest and the largest measured value for the same subject was .98. Together these data also indicated that the vmHRV values for an individual variated little across a two-week period, but that some considerable deviations from this pattern occurred.

Table 2. *Overview of VmHRV (LnRMSSD) Values in Sample One on First Assessments, Mean and Range of the 13 Assessments*

Subject	1. assessment	*M* (1.-13. assessment) (*SD*)	Range (difference)
1	2.90	2.93 (0.31)	2.48 - 3.57 (1.09)
2	3.73	3.78 (0.18)	3.39 - 4.02 (0.63)
3	3.99	4.01 (0.31)	3.57 - 4.65 (1.08)
4	4.59	4.81 (0.34)	4.10 - 5.27 (1.17)
5	4.29	4.36 (0.26)	3.65 - 4.59 (0.94)
6	4.29	4.14 (0.28)	3.61 - 4.56 (0.95)
7	4.06	4.05 (0.22)	3.63 - 4.38 (0.75)
8	2.83	3.52 (0.31)	2.83 - 3.96 (1.13)
9	4.01	4.37 (0.15)	4.01 - 4.56 (0.54)
10	4.28	4.75 (0.36)	4.21 - 5.27 (1.07)
11	4.46	4.16 (0.40)	3.23 - 4.61 (1.39)
Total (*M*)	3.95	4.08 (0.34)	3.51 - 4.41 (0.98)

Note. n = 11. VmHRV (LnRMSSD) = Vagally mediated heart rate variability (Log transformed root mean square of the successive differences).

Correlational analyses on the study variables

Vagally mediated heart rate variability (vmHRV) in sample two did not correlate significantly with any of the included study variables, except for self-reported physical activity (see Table 3), indicating non-existent or indirect associations between vmHRV and symptoms of anxiety, depression, maladaptive metacognitions and resilience factors, as well as sleep quality. Further, with the exception of the MCQ-30 and self-reported physical activity, all the other study variables were significantly correlated.

Self-reported physical activity correlated weakly and positively with vmHRV and the RSA, indicating that higher levels of physical activity are associated with higher levels of VMHRV and resilience. Further, self-reported physical activity was very weakly and negatively correlated with self-reported sleep quality, and weakly with the GAD-7 and the PHQ-9, indicating that higher levels of physical activity are associated with better sleep quality and lower levels of anxiety and depression.

Subjective sleep quality was found to be correlated moderately and positively with the GAD-7 and the PHQ-9, weakly and positively with the MCQ-30, as well as moderately and negatively with the RSA, indicating that better sleep quality is associated with lower levels of anxiety, depression, maladaptive metacognitions, and higher levels of resilience.

The GAD-7 correlated strongly and positively with the PHQ-9 and the MCQ-30, and moderately and negatively with RSA, indicating that higher levels of anxiety are associated with higher levels of depression, maladaptive metacognitions and lower levels of resilience. In addition, the PHQ-9 correlated moderately and positively with the MCQ-30 and moderately and negatively with the RSA, indicating that higher levels of depression are associated with higher levels of maladaptive metacognitions and lower levels of resilience. Lastly, the MCQ-30 and the RSA correlated moderately and negatively, indicating that higher levels of maladaptive metacognitions are associated with lower levels of resilience.

Table 3. *Intercorrelations Among the Study Variables.*

	VmHRV (LnRMSSD)	Physical activity	Sleep quality	GAD-7	PHQ-9	MCQ-30	RSA
Physical activity	.33**						
Sleep quality	-.07	-.17*					
GAD-7	-.10	-.20**	.47**				
PHQ-9	-.11	-.25**	.57**	.75**			
MCQ-30	-.12	-.13	.37**	.64**	.55**		
RSA	.11	.31**	-.42**	-.45**	-.56**	-.51**	

Note. n = 201. VmHRV (LnRMSSD) = Vagally mediated heart rate variability (Log transformed root mean square of the successive differences), GAD-7 = Generalized Anxiety Disorder Scale, PHQ-9 = Patient Health Questionnaire, RSA = Resilience Scale for Adults, MCQ-30 = Metacognitions Questionnaire. *p <.05, ** p <.01

Path analyses

In the correlation analyses, vmHRV was found to correlate significantly only with physical activity. However, physical activity was significantly correlated with all the other variables except maladaptive metacognitions. This could indicate that vmHRV is indirectly, more than directly, associated with symptoms of anxiety and depression. Thus, two path models were hypothesised to investigate the relationships between the variables. Path model 1 (Figure 1) focuses on the relationship between anxiety symptoms, physical activity, sleep quality, maladaptive metacognitions, resilience and vmHRV. In path model 2 (Figure 2), anxiety symptoms are replaced with depressive symptoms.

The hypothesised path model for anxiety symptoms (Figure 1) showed the following fit indices: χ^2=2.5, p = .78; RMSEA = .000; CFI = 1.000; TLI = 1.028; SRMR = .019. These fit indices indicate that the path model has a good fit to the data. Further, the hypothesised path model for symptoms of depression (Figure 2) showed the following fit indices: χ^2=2.4, p = .79; RMSEA = .000; CFI = 1.000; TLI = 1.028; SRMR = .019. These fit indices indicate that path model 2 also has a good fit to the data.

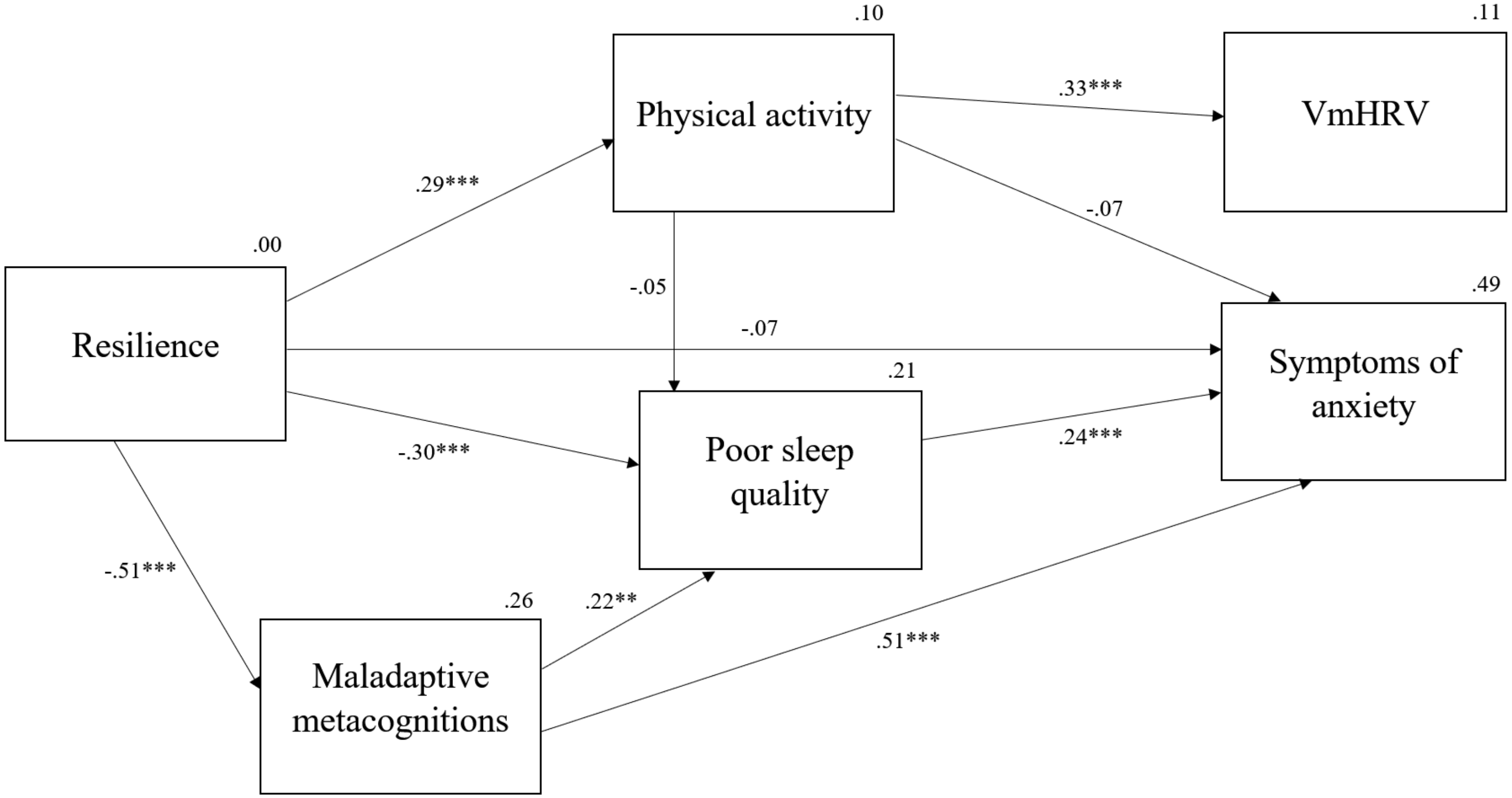
Both path models explained 11% of the variance in vmHRV. Further, path model 1 explained 49% of the variance in anxiety symptoms, and path model 2 explained 51% of the variance in symptoms of depression. Although physical activity initially was correlated to vmHRV, resilience, sleep quality and anxiety symptoms, the path models only indicate direct relationships to vmHRV and resilience. For both models, resilience had a moderate direct effect on physical activity (r = .29, p < .01), and an indirect small effect on vmHRV (r = .11, p < .01) via physical activity. Physical activity had a moderate direct effect on vmHRV (r = .33, p < .01).

The path model for anxiety symptoms showed that resilience did not have a direct effect on anxiety symptoms, but it had a moderate-to-large indirect effect on anxiety symptoms via maladaptive metacognitions and poor sleep quality (r = -.38, p < .001). On the other hand, resilience had a small-to-moderate direct effect on symptoms of depression in model 2 (r = .25, p < .001), in addition to a moderate indirect effect on symptoms of depression via maladaptive metacognitions and poor sleep quality (r = -.31, p < .01).

For both models, resilience had a large direct effect on maladaptive metacognitions (-.51, p < .001) and a moderate direct effect on sleep quality (r = -.30, p < .001). In model 1, maladaptive metacognitions had a large direct effect on anxiety symptoms (r = .51, p < .01) and a very small indirect effect via poor sleep quality (r = .05, p < .01). Poor sleep quality had a small-to-moderate direct effect on anxiety symptoms (r = .24, p < .01). In model 2, maladaptive metacognitions had a moderate direct effect on symptoms of depression ($r = .28$, $p < .001$), and a very small indirect effect on symptoms of depression via poor sleep quality ($r = .08$, $p < .01$).

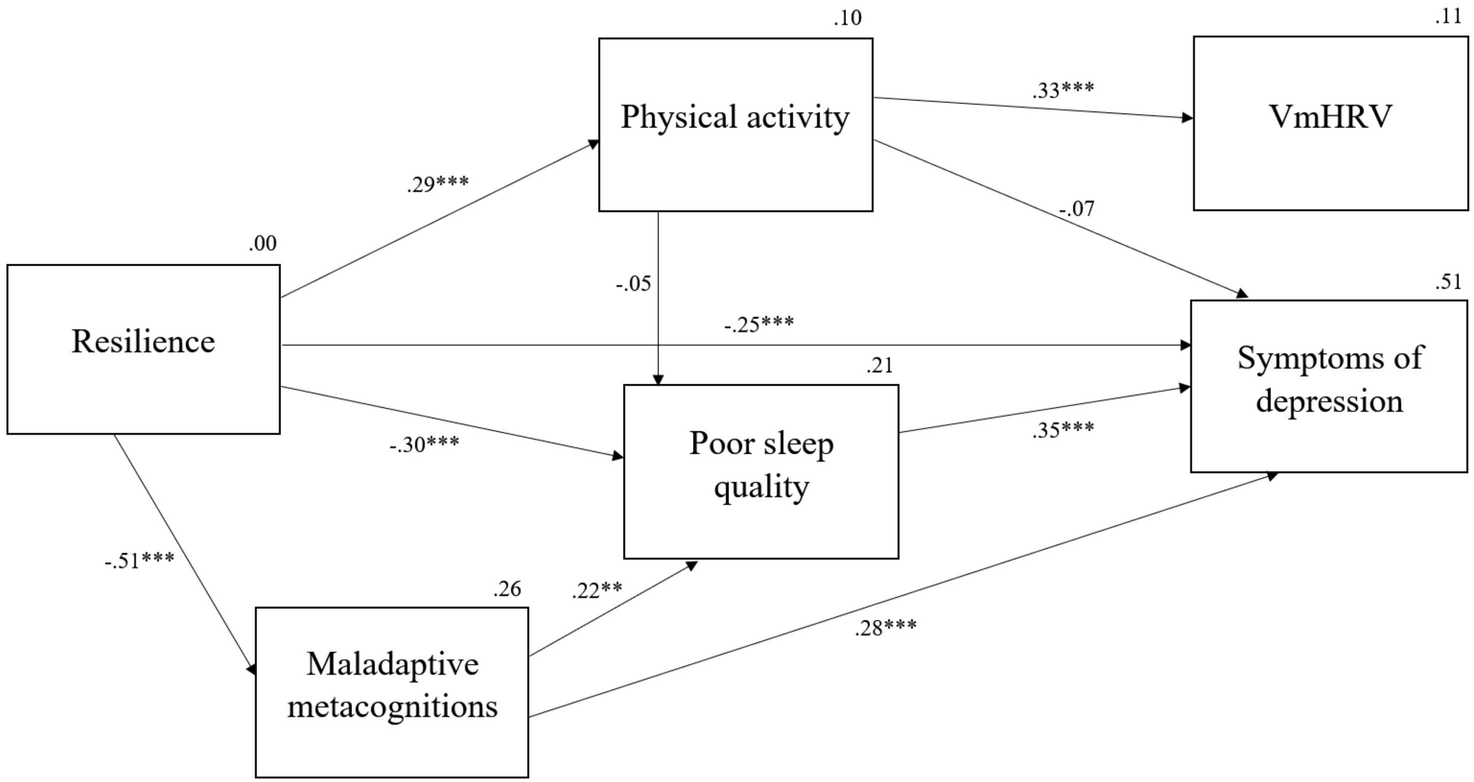
The explained variance for all dependent variables is reported in Figure 1 and 2.

Figure 1. Path model 1 - Analysis of resilience, maladaptive metacognitions, poor sleep quality and physical activity in relation to vmHRV and symptoms of anxiety.



Note. n = 201. Resilience is assessed with the Resilience Scale for Adults (RSA), maladaptive metacognitions with the Metacognitions questionnaire (MCQ-30), physical activity and sleep quality with single self-report questions, vmHRV with ultra-short term time domain PPG technology, and symptoms of anxiety with the Generalized Anxiety Disorder Scale (GAD-7). * p <.05, ** p <.01, ***p < .001

Figure 2. Path model 2 – Analysis of resilience, maladaptive metacognitions, poor sleep quality and physical activity in relation to vmHRV and symptoms of depression.



*Note. n = 201*Resilience is assessed with the Resilience Scale for Adults (RSA), maladaptive metacognitions with the Metacognitions questionnaire (MCQ-30), physical activity and sleep quality with single self-report questions, vmHRV with ultra-short term time domain PPG technology, and symptoms of depression with the Patient Health Questionnaire (PHQ-9). * $p < .05$, ** $p < .01$, ***$p < .001$

The current HRV values compared to other studies

Evaluation of the vmHRV data is difficult, due to significant variations in HRV with respect to e.g. age, physical health and measuring method. The current study applied novel equipment for measurement (the ithlete finger sensor and application), which makes evaluation of the current HRV data even more problematic. However, to get an indication of whether the current HRV data set was suited for analysis, results were compared to studies with comparable samples (healthy subjects with the approximate same age), assessment methods or study designs. In Table 4, age, sample size, assessment method, means and/or ranges for vmHRV data are displayed from six different studies along with data from the current study. The table is meant to be informational, and it is emphasised that it does not represent a thorough review of HRV data. Comparing the means and standard deviations given by Melanson (2000), Zhang (2007) and Zulfiquar et al. (2010) to the current study, there is indication that the difference between the current HRV data and the HRV values found in these studies are small (d = -.14 in comparison to Melanson, 2000; d = .16 in comparison to Zhang, 2007; d = .10 in comparison to the age group 10-19 years, measured by Zulfiquar et al., 2010; and d = .23 in comparison to the age group 20-29, measured by Zulfiquar et al., 2010). However, comparison to three other studies is not enough to give clear indications on the reliability of the HRV data. With further inspection of the study findings in Table 4, there is indication that the current HRV data are within the higher range of HRV values found. Possible explanations for this are reviewed in the discussion.

Table 4. *Heart Rate Variability (LnRMSSD) Data from the Current- and Comparable Studies*

	Melanson (2000)	Acharya et al. (2004)	Zhang (2007)	Zulfiquar et al. (2010)	Zulfiquar et al. (2010)	Nunan et al. (2010)	Baek et al. (2015)	The current study (2019)
Age range	Not given	25 ± 10 years	20-29	20-29	10-19	18+ years	20-29	18-29
Mean age (*SD*)	29.4 (3.1)	Not given	Not given	Not given	Not given	-	26.59 (2.04)	21.52 (2.75)
N	10	50	63	47	22	21,438	123	201
Assessment method	10-minute ECG	20-minute ECG	Short-term	24-hour ambulatory ECG	24-hour ambulatory ECG	Short-term, paced breathing	Ultra-short-term PPG	Ultra-short-term PPG
Mean*	4.53(3.70)	Not given	3.78(3.30)	3.71 (2.77)	3.97 (2.77)	4.01 (not given)	Not given	4.16 (.41)
Range*	Not given	4.13 - 4.38	2.22 - 4.99	Not given	Not given	Not given	3.22 - 3.40	2.95 - 5.45

Note. * = LnRMSSD(*SD*). LnRMSSD = Log transformed root mean square of the successive differences. ECG = Electrocardiography. PPG = Photoplethysmography. Nunan et al. (2010) is a review of several studies.

Discussion

Summary of the main findings

The results were consistent with the first hypothesis, indicating that the first assessment of vmHRV could be considered a reliable representation of subsequent vmHRV assessments for the same individual within a time period of at least two weeks.

For the second hypothesis, results were not as expected, as vmHRV did not significantly correlate with symptoms of depression or anxiety, maladaptive metacognitions, resilience, or sleep quality. A significant and positive correlation was however found between vmHRV and physical activity ($r = .33$, $p < .001$). All associations were in the hypothesised positive or negative direction. With the exception of maladaptive metacognitions and physical activity, all other study variables were significantly correlated with each other. The finding that physical activity was correlated to vmHRV, symptoms of anxiety and depression, as well as resilience and sleep quality suggested a potential indirect relationship between vmHRV and mental health factors.

Proceeding from these correlational findings, two path models for anxiety and depression, respectively, were hypothesised. They demonstrated good fit indices. For both models, two paths with resilience as a common factor emerged. On the one side the path models showed that resilience, maladaptive metacognitions and subjective sleep quality together explained 49% of the variance in anxiety symptoms and 51% of the variance in symptoms of depression. On the other side the path models showed that resilience and self-reported physical activity explained 11% of the variance in vmHRV. Thus, even though vmHRV was not directly correlated to symptoms of anxiety and depression or any of the other mental health factors, the path models indicate that vmHRV is indirectly related to indicators of mental health and that resilience could be a key factor in this relationship.

For the third hypothesis, there is indication that the results are consistent with the expectations – that the difference between the current HRV data and the HRV values found in other comparable studies are small, even though they seem to be within the higher range of HRV values found. However, this is based on a comparison to five other studies and one review study and should therefore be interpreted with caution.

Implications of the findings

VmHRV measured in the resting state is by central researchers within the field (e.g. Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012) referred to as a measure that can be applied in research on individual differences, which implies that it is a relatively stable measure within a time period for an individual. Kleiger et al. (1991) found that assessment of resting state HRV for 14 individuals (age 25-55 years) was essentially constant for each individual within the 65 days of study. As this study sought out to measure vmHRV in a large sample, it was important to establish on beforehand whether vmHRV values assessed with the ithlete equipment in a resting state corresponded to expectations of stability. Data analysis of repeated measures in sample one gave support to the hypothesis, as high internal consistency between points of measurements was indicated, and the first assessments correlated highly with the mean of all 13 assessments. Even though the results were essentially in line with the expectations, the range in values for each subject (Table 2) show that some considerable deviations from the mean occur. For analysis in a large sample like the current (*n* = 201), these occasional deviations probably do not make a significant difference. However, in analysis of smaller samples one should be aware of deviations and careful to make inferences based on single measurements with the ithlete equipment.

The current study did not, in contrast to previous studies, demonstrate significant associations between HRV and symptoms of anxiety and depression. One alternative explanation for this could be that the HRV values or psychological symptom scores did not represent enough variation or that they were diverging in other ways. As reported, there are indications that the HRV values are within the higher range of what has previously been found, but that the differences between previous findings and the current are small. Thus, the HRV scores are considered applicable for analysis of the sample. As for the psychological symptom scores, the mean scores of anxiety and depression were in the minimal to mild ranges, indicating low levels overall of anxiety and depression in the current sample. However, the number of subjects scoring above cut-off for clinical depression and clinically significant anxiety in the sample is markedly higher than what was found in two German population studies on the PHQ-9 and GAD-7, respectively (Kocalevent, Hinz, & Brähler, 2013; Löwe et al., 2008). In the German sample of 5018 subjects (53.6% female, 14-92 years), 12% reported a score of 8 or higher (Kocalevent et al., 2013). Within the most comparable subsample to the current study, which was women aged 14-24 years (*n* = 272), 12% scored above cut-off. As for anxiety symptoms, approximately six percent reported a score above the suggested cut-off in the German sample of 5030 subjects (53.6% female, 14-92 years, Löwe et al., 2008). For the most comparable subsample, which was women aged 14-24 years (*n* = 260), the number was eight percent (Löwe et al., 2008). With referral to these findings; if there was a clear association between vmHRV and symptoms of depression and anxiety there are good reasons to expect the association to be found in the current data. Thus, the results indicate that vmHRV and symptoms of depression and anxiety might not be intimately associated. As previously stated, non-significant findings have also been demonstrated before, so the current finding is not unique. Also, studies that have found a significant association between HRV and symptoms of anxiety or depression have interesting results that can possibly explain the current non-significant association. An example is Licht et al. (2008), which is a study on a large sample (n = 2373) consisting of 774 individuals with remitted MDD, 1075 individuals with current MDD and 524 controls. Here it was found that depression was associated with significantly lowered heart rate variability, but the association appeared to be mainly driven by the effects of antidepressants. In the current study, only 3.5% reported use of antidepressants. To sum up, the correlational findings suggest that one should be careful not to overestimate the role of HRV, and possibly other physiological measures, in relation to mental health. However, interesting findings from the path analyses indicate that HRV could be indirectly related to symptoms of anxiety and depression through physical activity and resilience.

The path models showed that physical activity had no direct association to symptoms of anxiety or depression when resilience, maladaptive metacognitions and sleep quality were included in the model. Resilience was the only factor that was directly associated to physical activity. These results indicate that resilience function as a bridge between physical- (physical activity and HRV) and psychological variables (metacognitions, sleep quality and symptoms of anxiety and depression). Similar results have been shown in a study by Ho, Louie, Chow, Wong, and Ip (2015), which found that physical activity levels in adolescents were significantly correlated with mental well-being, and that resilience accounted for 60% of this relationship. Another example is a study by (Yoshikawa, Nishi, and Matsuoka (2016), where physical activity was found to affect depressive symptoms indirectly through social support and resilience. Thus, resilience could be especially interesting to study further when looking for potential biomarkers within the RDoC framework. One suggestion could be to study if some subscales of the RSA are particularly related to HRV. However, in the current data set there was not found a direct correlation between subscales of the RSA and vmHRV.

Maladaptive metacognitions could also be interesting to study further in relation to biomarkers, as it was closely related to especially resilience and anxiety symptoms, but also to sleep quality and symptoms of depression in the current models. Maladaptive metacognitions and poor sleep quality were the only direct and significant predictors associated with symptoms of anxiety. The finding that maladaptive metacognitions and poor sleep quality were the best predictors for symptoms of anxiety, indicate that they play an important role in explaining these symptoms. This is not surprising given that previous studies have shown that they are implicated in sustaining anxiety (see i.e. Johnson et al., 2018; Sun et al., 2017; Hertenstein et al., 2018) and further that the MCQ was developed based on data from patients with anxiety disorders (Wells & Cartwright-Hatton, 2004). Metacognitions and sleep quality have also been implicated in explaining depressive symptoms (Solem, Hagen, Hoksnes, & Hjemdal, 2016; Hertenstein et al., 2018), which was supported by the direct effects found in the current study (Figure 2).

Moving on from the path analyses, the following paragraphs will go through research on HRV assessment with the goal of providing a better understanding of why the current HRV data seem to be a little higher than what has been generally found in other comparable studies. To start with the impact of age, studies have generally found a decline in vagally mediated HRV with increasing age (e.g. O'Brien, O'Hare, & Corrall, 1986). Zulfiquar et al. (2010) found a rapid decline in vmHRV between the ages of 20 and 50. As mentioned in the introduction, this study sought to avoid a large age effect on the data and thus limited the age range to 18-29 years. When comparing the data with other studies of healthy subjects within the same age range, however, we must also consider that the mean age of the current sample was as low as 21.5 (*SD* = 2.8) years. Therefore, it might be just as applicable to compare RMSSD values with those reported from the age range 10-19 years as the age range 20-29 years. Looking at this age range (10-19) in the study by Zulfiquar et al. (2012), the divergence to the current data is not as large.

Further, as reported in Table 4, Melanson (2000) is an example of a study that reports higher HRV values than found in the current data set. Nunan, Sandercock and Brodie (2010) suggest that the high RMSSD values reported by Melanson (2000) might be explained by the combined effect of young, trained individuals with higher baseline vagal tone and the use of supine and paced breathing protocols. Looking at the self-reported levels of physical activity in the current study, about 80% report an activity level of 4 or higher on a scale from 1-10, indicating that a large amount of the sample are moderately to highly physically active. However, as found by Prince et al. (2008) the validity and reliability of self-report measures of physical activity can be problematic. They found that self-report measures were both higher and lower than directly measured levels of physical activity. Thus, interpretation of these findings must be done with caution.

The current study also applied assessment equipment with a paced and slow breathing pattern (7.5 breaths per minute). Brown, Beightol, Koh and Eckberg (1993) found that respiration parameters strongly influence HRV and they recommend that respiration must be controlled in order to interpret HRV power spectra. Relatively small changes in natural breathing rates, in the region between 7.5-15 breaths per minute can cause quite significant changes in measured HRV. Slower breathing patterns caused higher HRV. Further, they found that the breathing rate and depths used did not alter the net amount of autonomic sympathetic or parasympathetic tone. In other words, carefully designed breathing patterns need not cause stress or alter the autonomic state of the person being measured. This indicates that by using a slow and controlled breathing pattern you can maximise HRV at breathing rate, without disturbing the body's underlying autonomic balance, which is what we want to measure. Neither Baek et al. (2015), Zulfiquar (2010), Acharya et al. (2004) or Zhang (2007) report having controlled respiration during HRV assessment. Thus, it might be that the higher levels of HRV in the current data set can be explained by the controlled, slow breathing pattern.

Limitations and strengths

The current study has limitations and strengths that are important to consider. The study sample was selected within a limited age span which prevents generalisation to other age groups, especially considering the robust connection between age and HRV (Zhang, 2007). On the other side, the selection of a particular age span also enabled studying specific associations in this age group with less impact from age as a variable. Further, when measuring HRV, as previously discussed, results have been shown to vary depending on method of measurement, indicating that we should be cautious in interpreting results based on different methods of measurement. However, large and significant correlations have been demonstrated between the method of measurement in the current study, and e.g. ECG measurements (Esco et al., 2017).

The current sample was not selected based on diagnostic categories as the purpose of the study was to examine relationships in a large age-selected student sample without cardiovascular diseases. One could argue that this makes the sample unsuitable to investigate relationships between HRV, anxiety, and depression. However, it could also be considered as a strength considering that the majority of studies on HRV and mental health have been conducted on selected samples, making the research vulnerable to selection bias (Galbaud du Fort, Newman, & Bland, 1993). Further, as previously discussed a substantial proportion of the current sample scored above cut-off values for depression and anxiety compared to large population-based studies in Germany (Kocalevent et al., 2013; Löwe et al., 2008) suggesting that a large group in our sample experienced symptoms of anxiety and depression in the clinical range. Participant`s levels of depression, anxiety, sleep, resilience, metacognitions, and other study variables were solely based on self-report. No structured clinical evaluations were conducted. However, the current study also included an objective measure (HRV) which could be compared to self-reported variables of interest. Sleep and physical activity were each derived from a single item, in contrast to the other self-reported variables which were based on well validated and complete self-report inventories. Future studies could therefore utilise full inventories for these variables as well in replicating the findings. It is important to mention that the current study utilised a cross-sectional design, and therefore no causal inferences can be made. Future studies could utilise longitudinal designs to be able to test hypothesised causal mechanisms. The study is the first to our knowledge to measure HRV using the ithlete app and equipment in a large age-selected sample without cardiovascular diseases. The sample HRV-scores could prove valuable as it could be utilised as a control in comparison to in example clinical populations in future studies. However since the current study did not find significant associations with the included mental health factors, other studies using different ways of measuring HRV should also be explored further in similar samples.

Conclusion

The study demonstrated that vmHRV scores were stable for 11 participants measured over a two-week period. Further, vmHRV could be successfully measured in a large group in a time-efficient way as described in the study. In contrast to expectations, vmHRV was not significantly correlated with symptoms of anxiety and depression, resilience, metacognitions or sleep quality in the current study. However, vmHRV was weakly correlated in the expected direction to self-reported general physical activity level, which again was correlated with symptoms of anxiety and depression suggesting indirect relationships between vmHRV and symptoms of anxiety and depression. The path analysis showed that resilience in particular appeared to function as a bridge between the physical and mental health-factors included in the study. Maladaptive metacognitions were found to be especially important in relation to symptoms of anxiety. Both resilience, maladaptive metacognitions and poor sleep quality were clearly associated with depression. Future studies could try to replicate the findings using other methods of measuring vmHRV and demonstrate the associations in longitudinal study-designs.

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