Resting heart rate variability, emotion regulation, psychological wellbeing and autism symptomatology in adults with and without autism

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Abstract

Heart rate variability (HRV) has been separately shown to be associated with ASD symptomatology, psychological wellbeing and emotion regulation (ER) in specific samples consisting of either individuals with ASD, those without ASD, or combined. However, no study has examined these constructs together or incorporated habitual ER strategy use. Hence, the aim of this study was to examine the relationships between resting HRV, ASD symptomatology, ER strategy use (reappraisal and suppression), and psychological wellbeing (anxiety, depression and positive wellbeing) in a combined sample of adults with and without ASD. Twenty-four adults with ASD ($M_{\text{age}} = 31.36; SD_{\text{age}} = 14.84$) and twenty without ASD ($M_{\text{age}} = 35.45; SD_{\text{age}} = 12.19$) completed the ER Questionnaire (ERQ), Diagnostic and Statistical Manual of Mental Disorders-5 Cross-cutting Dimensional Scale, Patient Health Questionnaire-9, Warwick-Edinburgh Mental Well-being Scale, and Autism-Spectrum Quotient-Short. Participants’ resting HRV data were also collected via short-term electrocardiogram. Self-reported use of reappraisal was associated with higher resting HRV. Additionally, reappraisal predicted variance in all three HRV indices above and beyond ASD symptomatology and medication use. These preliminary findings can inform the design of future studies to determine the extent to which reappraisal impacts autonomic flexibility.

Keywords: Cognitive reappraisal, emotion regulation, psychological wellbeing, anxiety, depression, heart rate variability, autism spectrum disorder
1 Introduction

Anxiety disorders and depression are the most prevalent mental health conditions (Kessler et al., 2005), affecting 14.5% to 33.7% and 8% to 12% of the general population, respectively (Andrade et al., 2003; Bandelow & Michaelis, 2015). In addition to their high prevalence, both disorders have significant negative impact on physical and somatic health (Bhattacharya et al., 2014; Murray & Lopez, 1997; Patten et al., 2008; Scott et al., 2007; Vogelzangs et al., 2010). For example, depression has been projected as one of the top contributors to disease burden in 2020, second to coronary artery disease (Murray & Lopez, 1997), and anxiety disorders increase the risk of coronary heart disease by almost 3-fold and comorbid anxiety/depression by 3.6 fold (Vogelzangs et al., 2010).

Anxiety and depression are particularly prevalent in individuals diagnosed with autism spectrum disorder (ASD), irrespective of their age, with up to 70% of individuals experiencing clinically significant levels of anxiety and up to 84% with depression (Croen et al., 2015; Kim et al., 2000; Lainhart, 1999; Lugnegard et al., 2011; Hofvander et al., 2009; Mazzone et al., 2012; Muris et al., 1998). As in other populations, anxiety and depression symptoms have a major negative impact on the health of individuals with ASD, as evidenced by the associations with greater loneliness, behavioural problems, lower quality of life, sleep problems and suicidal ideation (Hedley et al., 2017; Farrugia & Hudson, 2006; Richdale & Baglin, 2015; Stewart et al., 2006; White & Roberson-Nay, 2009).

One of the key risk factors linked to the development and maintenance of affective and behavioural problems in the general population (Aldao et al., 2010; Gross and Jazaieri, 2014; McLaughlin et al., 2011), and more recently in ASD (Mazefsky et al., 2013; Weiss et al., 2014; White et al., 2014), is deficits in the ability
to regulate emotions. Emotion regulation (ER) is the goal-directed process of modifying and responding to emotions that are experienced in everyday life (Eisenberg & Spinrad 2004; Thompson 1991). There is a repertoire of ER strategies that can be chosen and implemented (Bonanno & Burton, 2013), and individuals vary in their capacity to regulate emotions and their strategy preferences (Gross & John, 2003; Sheppes et al., 2014). Two strategies for regulating emotions that have been most robustly studied are cognitive reappraisal, which involves re-interpreting a situation to change the way one feels about it (Lazarus & Alfert, 1964), and expressive suppression, which involves inhibiting the expression of emotions (Gross & Levenson, 1993). Extensive research has been conducted to examine the consequences of both strategies and, overall, it has been concluded that reappraisal is a more adaptive strategy for regulating emotions than suppression (Butler et al., 2003; Campbell-Sills et al., 2006; Ehring et al., 2010; Garnefski et al., 2002; Gross & John, 2003; Gross, 1998; Gross & Levenson, 1993; Gross & Levenson, 1997; Mauss et al., 2007; Richards & Gross, 1999; Richards & Gross, 2000; Richards et al., 2003; Wenzlaff and Luxton, 2003).

One common factor that connects anxiety and depression with emotion dysregulation is heart rate variability (HRV), a reliable marker of autonomic activity (Malik, 1996). The next section provides a brief overview of the literature on HRV in the general population and its relationship with psychological health. The association between HRV and ER in predicting mental health is also discussed, highlighting its relevance for understanding the frequency and severity of anxiety and depression reported in ASD.
1.1 Heart rate variability and psychological wellbeing

HRV represents the variation in the interval between consecutive heartbeats and is most commonly measured via short- or long-term electrocardiogram (ECG) recordings. Cardiac vagal control can be measured via respiratory sinus arrhythmia (RSA), the high frequency heart rate variability associated with the respiratory cycle (Berntson et al., 1997). High HRV represents a sign of autonomic flexibility, and has been shown to protect against future cardiac events (e.g., Tsuji et al., 1996). In contrast, low HRV predicts both risk of coronary heart disease (e.g., Dekker et al., 2000) and risk of mortality (e.g., La Rovere et al., 2003).

Extensive research demonstrates the connections between low HRV and concomitant psychological disorders, particularly anxiety and depression. There are three comprehensive meta-analyses of the relationship between HRV and anxiety (Chalmers et al., 2014) and depression (Kemp et al., 2010; Rottenberg, 2007) in physically healthy individuals. The findings indicate that lower resting RSA is associated with increased symptoms of depression (Rottenberg, 2007), and lower resting HRV is associated with both depression (Kemp et al., 2010) and anxiety (Chalmers et al., 2014). Extending findings beyond anxiety and depression, a recent meta-analysis by Alvares and colleagues (2016) demonstrated reduced HRV in patients with a wide range of mental health conditions (mood, anxiety, psychosis and substance dependent disorders) relative to controls.

Psychotropic medications have been shown to impact on the cardiovascular system. There is ample evidence from both empirical studies and reviews to conclude that the use of tricyclic antidepressants is associated with lower HRV (e.g., Alvares et al., 2016; Kemp et al., 2010; Lehofer et al., 1997; Rechlin et al., 1994). However, the impact of other antidepressants is currently inconclusive, for example, there was an
active debate on the effects of selective serotonin reuptake inhibitors (SSRIs). In their meta-analytical review, Kemp et al. (2010) found that SSRIs are associated with benign cardiac effects whereas in a longitudinal study, Licht et al. (2010) concluded that tricyclic antidepressants, SSRIs and noradrenergic and specific serotonergic antidepressants (NaSSAs) decreased RSA. Kemp et al. (2011) suggested several reasons for Licht et al.’s findings including the analytical approach used and methodological issues. Furthermore, van Zyl et al. (2008) found that SSRIs increased one HRV measure in studies with short recording intervals. Finally, certain antipsychotic medications such as clozapine also have varying effects on HRV (e.g., Alvares et al., 2016; Silke et al., 2002).

1.2 Heart rate variability as a biomarker of emotion regulation

According to the Polyvagal Theory of emotions (Porges, 1997), cardiovascular control is associated with emotion regulatory capacity and in turn determines socio-communicative behaviours. Thus, researchers have suggested that HRV is a physiological indicator of the capacity to regulate emotions (Appelhans & Luecken, 2006; Thayer & Lane, 2000). Several empirical studies have demonstrated that higher resting HRV or RSA are associated with better emotion regulation and use of more constructive coping strategies (Fabes & Eisenberg, 1997; O’Connor et al., 2002) and lower resting HRV is associated with use of less constructive strategies (Fuller, 1992; Pauls & Stemmler, 2003; Sgoifo et al., 2003).

Only two studies, both with female samples, have examined the relationships between HRV and the use of reappraisal and suppression. Butler et al. (2006) found that women who were asked to either suppress or reappraise their emotions during face-to-face interactions showed a greater increase in RSA than women who were not prompted to use specific ER strategies. In the second study where female
undergraduate students viewed an anger-inducing video, participants who were
instructed to reappraise prior to watching the video showed increased HRV whereas
those who were asked to either suppress or simply watch the video showed no such
HRV increases (Denson et al., 2011). The authors concluded that the use of
reappraisal might result in greater autonomic flexibility in situations that trigger
anger. These two studies measured participant HRV before and after exposure to the
experimental stimuli under specific conditions (i.e., suppress, reappraise, or no ER
prompt). In light of these findings, it seems relevant to characterise the relationships
of the habitual use of reappraisal and suppression with resting HRV. However, to our
knowledge, no research to date has addressed this in either the general or ASD
populations.

1.3 Relationship of heart rate variability with autism severity, psychological
wellbeing, and emotion regulation

Findings on the associations between ASD symptom severity and resting HRV
have largely depended on the sample used in studies. For example, using a combined
sample of children with and without ASD, Neuhaus et al. (2014) found that parent-
reported ASD symptomatology was moderately associated with children’s baseline
RSA. In contrast, Klusek et al. (2013) examined the relationship between autism
severity and baseline RSA in their ASD and control groups separately, and only found
a significant association in the TD group. Research comparing resting HRV (and
RSA) in individuals with and without ASD has yielded mixed results. Some studies
report reduced resting levels in ASD (e.g., Guy et al., 2014; Mathewson et al., 2011),
while others have found similar resting levels in the two groups (e.g., Levine et al.,
2012; Sheinkopf et al., 2013; Toichi & Kamio, 2003).
Research has also demonstrated a relationship between resting RSA and psychological wellbeing in combined samples of children with and without ASD. Guy et al. (2014) showed higher parent-reported anxiety symptoms were correlated significantly with lower baseline RSA. Similarly, Neuhaus et al. (2014) also found baseline RSA to be correlated significantly with internalising and externalising symptoms (including measures of anxiety and depression) reported by parents. However, the relationship between resting HRV and psychological wellbeing has not been examined in adult samples.

In addition to the high prevalence of anxiety and depression in ASD (American Psychiatric Association 2013; Croen et al. 2015; Totsika et al. 2011), individuals with ASD also experience more ER difficulties, and either self-report or demonstrate a less adaptive pattern of ER strategy use (e.g., Bruggink et al. 2016; Samson et al., 2012). Based on a review of empirical work in ER, the higher prevalence of internalising symptoms in ASD appears linked to the habitual use of adaptive or/and maladaptive ER strategies (Cai et al., 2018). Based on the research summarised, it is possible that either AS symptom severity, psychological wellbeing, emotion regulation strategy use, or a combination of these are related to resting HRV, however these constructs have never been examined together.

1.4 Current study
Given their dimensional nature, it is increasingly recognised that in order to understand processes and mechanisms underlying specific mental health symptoms it is necessary to explore shared biological, cognitive, neural and behavioural elements across both normative and clinical populations (Insel et al., 2010). Autonomic nervous system dysfunction is suggested to be a marker for both psychological and physiological disorders (Alvares et al., 2016; Appelhans & Luecken, 2006). In
addition, emotion dysregulation has been shown to be a trans-diagnostic process associated with a range of mental health disorders (Aldao et al., 2016; Gross & John, 2003). Importantly, variations across both autonomic nervous system function and ER are observed in the general population. Therefore in the current study we adopted a dimensional approach to examine these constructs in a sample of adults with and without ASD. A similar approach has been used in other HRV (and RSA) research in autism (e.g., Neuhaus et al., 2014).

The aim in the current study was to examine the relationships between ASD symptomatology, ER (reappraisal and suppression), resting HRV and psychological wellbeing (anxiety, depression and positive wellbeing) in a combined sample of adults with and without ASD. Based on existing findings, we hypothesised that lower ASD symptomatology, psychological wellbeing, specifically higher positive aspects of psychological wellbeing and lower symptoms of anxiety and depression, and greater use of reappraisal and/or lower use of suppression would be associated with higher resting HRV. We were also interested to discover which of these variables predicted resting HRV.

2. Methods

2.1 Participants

Twenty-four individuals with ASD and twenty control individuals with intelligence quotients (IQ) > 80 participated in this study (see Table 1 for demographic information). All participants in the ASD group self-reported an ASD clinical diagnosis. The existence of an ASD diagnosis was an exclusionary criterion for the control group. Participants with mental health conditions were not excluded from this study, given that the scope of the study included examining individual
differences in psychological wellbeing. Any individuals with the following physical health conditions were excluded from the study: coronary artery disease, atherosclerosis, stroke, hypertension, heart failure, aortic dissection and aneurysm, myocarditis and pericarditis, cardiomyopathy, cardiac dysrhythmia and tachycardia, heart valve diseases, shock, vasculitis and other heart diseases.

2.2 Measures

2.2.1 Online measures

Demographics. A series of questions captured information regarding gender, date of birth, ASD diagnosis and year of diagnosis, co-morbid mental health conditions, medications taken in the past two weeks and ethnic background.

ASD symptoms. The Autism Spectrum Quotient (AQ-Short; Hoekstra et al., 2011) is a 28-item abbreviated version of the full 50-item AQ screening questionnaire (Baron-Cohen et al., 2001) relating to behaviours associated with ASD. Each item is rated on a 4-point scale from definitely agree to definitely disagree. A score above 65 has a sensitivity of .97 and a specificity of .82 for ASD, comparable to the full AQ (50 items). Correlation with the 50-item AQ has been shown to be very high, with r’s ranging from .93 to .95 (Hoekstra et al., 2011).

Habitual use of reappraisal and suppression. The Emotion Regulation Questionnaire (ERQ; Gross and John, 2003) is a 10-item self-report measure designed to assess the frequency of reappraisal (6 items) and suppression (4 items) use for both positive and negative emotions. The ERQ has been used previously with participants with ASD (e.g., Samson et al., 2012; Samson et al., 2015). Each item is rated on a 7-
point scale ranging from strongly disagree to strongly agree. A two-factor structure originally reported by Gross and John (2003) has subsequently been replicated in both exploratory and confirmatory factor analytic studies, with both factors showing adequate internal consistency; Cronbach’s alpha = .73-.76 for the suppression and .79-.82 for the reappraisal subscales (Melka et al., 2011; Moore et al., 2008).

**Anxiety symptoms.** The DSM-5 Cross-cutting Dimensional Scale (DSM-5 CROSS-D; Lebeau et al., 2012) is a 10-item self-report questionnaire designed to assess the presence of any anxiety symptoms. Each item is rated on a 5-point scale ranging from never to all of the time. The cutoff score for clinically significant anxiety is 14 (Beesdo-Baum et al., 2012), with both sensitivity and specificity of .73.

**Depression symptoms.** The Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001) is a 9-item, norm referenced questionnaire designed to screen for the presence of depression in general and clinical populations. Each item is rated on a 4-point scale ranging from not at all to nearly every day. Scores of 20, 15, 10 and 5 represent severe, moderately severe, moderate and mild depression respectively. A score of 10 or above had a sensitivity of .88 and a specificity of .88 for major depression (Kroenke et al., 2001).

**Positive psychological wellbeing.** The Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS; Tennant et al., 2007) is a 14-item scale of psychological wellbeing covering both hedonic and eudaimonic aspects of positive wellbeing including positive affect (feelings of optimism, cheerfulness, relaxation), positive functioning (energy, clear thinking, self-acceptance, personal development, competence and autonomy) and satisfying interpersonal relationships. Each item is rated on a 5-point scale ranging from none of the time to all of the time and all items are worded positively.
In this study, the internal consistency was adequate for ERQ-S ($\alpha = .67$) and ranged from good to excellent for AQ-Short ($\alpha = .94$), ERQ-R ($\alpha = .87$), DSM-5 CROSS-D ($\alpha = .92$), PHQ-9 ($\alpha = .91$), and WEMWBS ($\alpha = .94$).

2.2.2 Cognitive assessment

The Wechsler Abbreviated Scale of Intelligence-Second Edition (WASI-II; Wechsler, 2011) is a reliable measure of cognitive ability and consists of four subtests: Vocabulary, Similarities, Block Design, and Matrix Reasoning. The entire WASI-II requires 30 minutes to administer. The subtests have high internal consistency (Split-half coefficient ranging from .87 to .92) and good test-retest reliability (Pearson’s $r$ ranging from .79-.94).

2.2.3 Behavioural assessment

The Autism Diagnostic Observation Schedule-2nd Edition (ADOS-2; Lord et al., 2012) is a semi-structured, standardised assessment of social interaction, communication, restricted and repetitive behaviours and imagination to evaluate individuals suspected of having ASD. Module 4 is used for assessing verbally fluent older adolescents and adults, administered face-to-face and requires up to 60 minutes to administer. Sensitivity and specificity of the newly revised algorithms for Module 4 is 90.5% and 82.2%, respectively (Hus & Lord, 2014).

2.3 Procedure

Ethics approval was obtained from La Trobe University’s Human Ethics Committee. Adult participants 18 years and over with ASD located in Melbourne were recruited via emails to members of Asperger’s Victoria and the ASD participant database of the Olga Tennison Autism Research Centre, as well as through researchers and other participants. Control participants were recruited through advertisements placed throughout building notice boards at La Trobe University as
well as through word of mouth by the researchers. Eight participants with ASD were recruited inter-state (Sydney and Brisbane) through two longitudinal studies: the Study of Australian School Leavers with Autism and the Australian Longitudinal Study of Adults with Autism.

Email screening occurred to exclude individuals with physical health conditions that may impact HRV. Eligible individuals read an information statement about the study and provided written, informed consent prior to attending an appointment, scheduled either at an office or in their own homes. Their HRV was measured first, after which they were offered a drink and snacks. They were then administered the WASI-II and participants with ASD completed Module 4 of the ADOS-2. The first author, who was trained in administration, conducted the ADOS-2. An independent researcher who is both a research reliable ADOS-2 assessor and a certified ADOS trainer coded all of the ADOS-2 videos.

All participants were sent an online survey link using Qualtrics (Qualtrics, 2014), a web-based tool for creating and conducting online surveys. The survey included demographic information and questionnaires about autism traits, psychological wellbeing and their habitual use of specific emotion regulation strategies.

2.3.1 Resting heart rate variability

A wide range of factors can influence HRV. Overall, HRV declines with age (O’Brien et al., 1986) and gender influences vary depending on the HRV measures used. For example, Agelink and colleagues (2001) found that young and middle-aged women showed both low frequency power and low frequency/high frequency ratio compared with age-matched men; however, no gender differences were observed in absolute high frequency power. HRV has a circadian rhythm, and also is affected by
medications for cardiovascular disease, hypertension, psychological disorders (see brief discussion in the Introduction), food and water intake, exercise, certain illnesses such as hypotension and bladder distension, consumption of caffeine and smoking (see Heathers, 2014 for a brief overview of the effects of these variables). Therefore, attempts were made in the current study to control these factors stringently where applicable.

An email containing guidelines for the HRV measurement was sent to all participants, who were also instructed not to ingest food, alcoholic beverages or caffeinated drinks for 12 hours prior to the scheduled assessment time. Individuals were also advised not to smoke and to avoid strenuous physical activity during this period. The ECG recording guidelines were also provided to reduce possible participant anxiety. These detailed what the recording process would entail and recommendations for shaving in order to reduce pain when ECG electrodes were removed as well as to ensure clearer ECG signals (applicable for male participants).

To reduce the impact of circadian rhythm effects on HRV data (e.g., Massin et al., 2000), the appointment was confined to a time window within 3 hours, as advised by Heathers (2014) and scheduled in the morning between 7:30am and 10:30am. During the appointment, HRV data were first obtained from an ECG recording device (Mega Electronics eMotion Faros 180° with 3 leads) for approximately 10 minutes. The sampling rate for ECG was set at 1000 Hz and electrodes were placed on the right arm, left arm and left leg positions as indicated in the eMotion Faros Series Manual (Mega 2015). Ambu WhiteSensor snap connector ECG electrodes were used. Participants were in a supine position and under dim lighting.

The ECG data were saved in European Data Format (EDF) and processed with Kubios Premium version 3.0.2. The ECG signals were visually inspected for
movements and a 5-minute segment with no or minimal movement was selected for each participant. These segments were analysed for time and frequency domain components with standard algorithms implemented in the Kubios software. Any artefacts and ectopic beats were automatically adjusted using the Kubios’ artefact correction algorithm (see Mega 2015, p36 for details). Trend components were removed using the smoothness priors approach (Tarvainen et al., 2002), with lambda set to 500. The default values for very low frequency (VLF; 0-0.04 Hz), low frequency (LF; 0.04-0.15 Hz), and high frequency (HF; 0.15-0.4 Hz) bands were used, aligning with the recommendations provided by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (henceforth termed as the Task Force; Malik, 1996).

2.4 Statistical analyses

Tests of normality using the Kolmogorov-Smirnov statistic were conducted and statistical approaches were chosen based on normality results. The analyses used to compare the ASD and control groups on FSIQ, age and gender were t-test, Mann-Whitney U test, and Chi-square test for independence.

Based on recommendations from the Task Force (Malik, 1996) and Heathers (2014), the time- and frequency-domain measures of resting HRV used in this study were HF, standard deviation of the normal-to-normal interval (SDNN), and square root of the mean of the sum of the squares of differences between adjacent normal-to-normal intervals (RMSDD). The absolute/raw HF spectral power was calculated using a Fast Fourier Transform (Kubios). The SDNN, RMSDD and HF values were log transformed prior to analyses due to the HRV data being positively skewed.

Informed by the dimensional approach (i.e., Insel et al., 2010), further analyses were conducted using the combined data. Pearson r correlation was used to
explore the associations between variables of interest and included psychotropic medication use (dichotomous variable: taking medication or not taking medication). Hierarchical regressions were also used to examine the extent to which reappraisal, medication use and ASD symptomatology accounted for the variances in the three HRV measures. Data were analysed using SPSS Statistics v21 for Mac and R version 3.3.0 was used for plotting the histogram. There were no missing data.

3. Results

3.1 ASD symptomatology

All individuals with ASD met criteria for ASD on one or both ADOS-2 (Lord et al., 2012) and the AQ-short (Hoekstra et al., 2011). Four individuals with ASD (16.7%) fell within the non-spectrum category based on their ADOS-2 Module 4 severity score, but they all scored > 65 (range 76 – 92) on the AQ-Short, and two participants who met ADOS-2 criteria for ASD had an AQ-short score ≤ 65 (i.e., 61 and 62). Five individuals in the control group (25%) scored > 65 on the AQ-Short (i.e., 66, 67, 71, 76, and 103).

3.2 Sample characteristics and medication use

The ASD and control groups were matched on full-scale IQ (FSIQ), \( t(42) = .05, p = .96, \eta^2 = .00; \) age, \( U = 231, z = -.21, p = .83, r = .03; \) and gender, \( \chi^2(1, 44) = .66, p = .42, \phi = .17. \) Seventeen individuals with ASD and one control participant self-reported a previous diagnosis of anxiety. Fourteen individuals with ASD and two control participants self-reported a previous diagnosis of depression. Nine individuals with ASD self-reported a diagnosis of attention deficit hyperactivity disorder and four self-reported a diagnosis of obsessive compulsive disorder. Some individuals had multiple co-morbid conditions. The self-reported medications used by participants in
this study were: agomelatine (1), benzodiazepines (2), carbamazepine (1), desvenlafaxine (2), duloxetine (1), methylphenidate (5), NaSSA (1), quetiapine (2), risperadone (2), SSRI (11) and valproic acid (1). No participants took tricyclic antidepressants or clozapine. Fifteen individuals with ASD (62% of ASD) and three control individuals (15% of controls) reported taking medications for mental health conditions at the time of study. One individual with ASD took agomelatine and carbamazepine, medications that have not been previously shown to reduce HRV, hence this individual was grouped with the other individuals who did not take psychotropic medications.

3.3 Preliminary analyses

The average percentage of artifacts removed across the whole sample was 0.60%. Tests of normality using Kolmogorov-Smirnov statistic showed that values on all three HRV measures significantly deviated from normality and were positively skewed. Hence, SDNN, RMSDD and HF values were log transformed. After the transformations, the distributions of all measures of interest were normal (see Table 2 for statistics).

Distributions of the AQ-Short scores (measuring ASD symptomatology) for the ASD and control groups are plotted in Figure 1. The histogram shows a bi-modal distribution that is consistent with the findings by Hoekstra et al. (2011), with the exception of one extreme outlier (AQ-Short = 103). This individual self-reported a diagnosis of bipolar II disorder.
3.4 Associations between variables of interest

Pearson r correlations showed that all HRV indices were moderately and positively associated with reappraisal (see Table 3). Additionally, RMSDD and HF were moderately correlated with ASD symptomatology. Point-biserial correlations showed that the three HRV indices were moderately associated with the use of medication (dichotomous variable).

Use of psychotropic medication was also significantly associated with lower age, higher symptoms of ASD, anxiety and depression, poorer positive wellbeing, greater use of suppression and lower use of reappraisal, with correlation strengths ranging between moderate and strong. The reappraisal scores were moderately and negatively associated with ASD symptomatology, anxiety and depression scores, and strongly positively associated with positive wellbeing scores. The suppression scores were positively associated with anxiety (strong) and depression (moderate) scores, and moderately negatively associated with positive wellbeing scores. Additionally, older age was moderately associated with both lower habitual use of suppression and decreased anxiety.

Based on the pattern of correlations noted above, three hierarchical multiple regression analyses were conducted with reappraisal and medication use as predictors of SDNN, RMSDD and HF. For the regression models containing RMSDD and HF, ASD symptomatology was also added as a predictor. The first regression analysis
examined the ability of reappraisal and medication use to predict SDNN. At step 1, reappraisal explained 18.4% of the variance in SDNN \((p = .004)\). Medication use was added at step 2 and the R square change for the model was not statistically significant, indicating medication use did not explain additional variance in SDNN. The total variance explained by the final model was 19.8%, \(F(2, 41) = 5.06, p = .011\). The second hierarchical regression analysis examined RMSDD as the dependent variable. Reappraisal explained 13.7% of the variance in RMSDD at step 1 \((p = .013)\), and ASD symptomatology and medication did not add significant amount of variance in the second step as indicated by the non-significant R square change. The model as a whole explained 18.5% of the variance in RMSDD, \(F(2, 41) = 3.03, p = .040\). The final hierarchical regression analysis showed a similar pattern of results. Reappraisal accounted for 11.1% of the variance in HF \((p = .027)\) and the R square change was not significant after adding ASD symptomatology and medication use at step 2. The final model explained 15.6% of the RMSDD variance, \(F(2,41) = 3.79, p = 0.031\).

4. Discussion

There were substantially more participants with ASD in our sample who reported having a clinical mental health condition such as anxiety, depression, and attention deficit hyperactivity disorder compared to the control group. Many more participants with ASD also reported being treated for these conditions via psychotropic medications (5:1 ratio). This aligns with a large body of work indicating the higher prevalence of mental health conditions in individuals with ASD (e.g., Wigham et al., 2017).

The aim of the current study was to characterise the relationships between resting HRV, ASD symptom severity, ER strategy use, and positive and negative aspects of psychological wellbeing in a sample of adults with and without ASD. We
adopted a dimensional approach by using the combined sample to examine whether or not these variables of interest were correlated, and which variables impacted HRV. These preliminary results indicate that cognitive reappraisal predicts resting HRV above and beyond use of psychotropic medications and ASD symptomatology.

4.1 Heart rate variability and its relationship with ASD symptom severity, psychological wellbeing, and emotion regulation

It was predicted that lower ASD symptomatology, higher positive aspects of psychological wellbeing and lower symptoms of anxiety and depression, greater use of reappraisal, and/or lower use of suppression would be associated with higher resting HRV. This hypothesis was partially supported by the study results. RMSDD and HF were found to be associated with ASD symptom severity, which supported previous work in children that showed baseline RSA was associated with ASD symptomatology (Neuhaus et al., 2014). SDNN is an estimate of the overall HRV. The HF component of HRV reflects parasympathetic activity as it is largely influenced by efferent vagal activity (Malik, 1996). RMSDD indexes HF heart rate oscillations (Shaffer & Ginsberg, 2017), hence it is highly correlated with HF (Kleiger et al., 2005). Since we found that both RMSDD and HF were both associated with ASD symptom severity, it is likely that individuals with ASD generally have reduced parasympathetic activation.

In contrast to our prediction, no measure of psychological wellbeing was associated significantly with any of the HRV indices. Past studies using combined samples of individuals with and without ASD found significant associations between baseline RSA and symptoms of anxiety and depression (Guy et al., 2014; Neuhaus et al., 2014), however these samples consisted of only children. Considering HRV decreases with age (O’Brien et al., 1986), it is possible that relationships between
HRV and psychological wellbeing differ in children and adults. Another possible explanation for these non-significant findings in the current research is the relatively small size of the sample. Future work of similar nature in a larger sample of adults is needed to confirm these patterns of relationships.

This study also showed the use of psychotropics was associated with lower resting HRV (all indices). Given that the majority of the individuals who were on medications took SSRIs in the current study, the findings align with Licht et al.’s (2010) work, which showed tricyclic antidepressants, SSRIs and noradrenergic and specific serotonergic antidepressants (NaSSAs) lowered HRV. Our finding did not support Kemp et al.’s (2010) conclusions. However, it is important to note that although it was important to consider the effects of medication in the scope of our research, the main focus of this research was not to examine the effects of psychotropic medications; hence the design of the study did not reflect a thorough examination of this. Future longitudinal studies on the effects of SSRIs on resting HRV are needed to assist with determining the effects of medications.

Finally, it was found that reappraisal but not suppression was associated with resting HRV and furthermore, reappraisal predicted HRV when the effects of medication and ASD symptom severity were controlled. As this is the first study to date to examine the relationship between resting HRV and habitual reappraisal and suppression use in any sample (ASD, non-ASD, or combined), it is difficult to provide direct comparison with the previous research which has employed experimental protocols in the general population. Previous studies have focussed on the effects of immediate changes in HRV after stimuli exposure during reappraisal, suppression, and no regulation-prompt conditions (i.e., Butler et al., 2006; Denson et al., 2011). However, some links can be drawn: in contrast to Butler et al.’s finding
that both reappraisers and suppressors showed a greater increase in RSA during face-to-face interactions, we did not find a relationship between habitual use of suppression and resting HRV. Our suppression finding is more in line with Denson et al.’s work reporting that reappraisers who watched an anger-inducing video showed increased HRV whereas suppressors did not show any increases in HRV. Our findings suggest that the long-term habitual use of reappraisal and suppression may be related differently to resting HRV compared to the relationships found with immediate changes in HRV in response to arousing external stimuli. Additionally, it is possible that ER may play a more important role than symptoms of anxiety and depression in their relationships with HRV.

We suggest that the individuals in our study who self-reported greater use of reappraisal may have more efficient prefrontal cortex function. This hypothesis is based on neuroimaging work in the general population. An experimental study on the neural bases of reappraisal and suppression found these strategies generated varying functional magnetic resonance imaging responses in the prefrontal cortex regions of participants during the early (0 - 4.5 seconds) and late (10.5 - 15 seconds) periods (Goldin et al., 2007). Reappraisal resulted in early responses whereas suppression produced late responses. When the two conditions were compared, the reappraisal condition produced greater down-regulation of negative-emotional experience. Considering these findings, it is likely that individuals who habitually reappraise may display a persistent pattern of neural activity that consists of increased early prefrontal cortex responses along with reduced late amygdala and insula responses, resulting in subsequent changes in their experience of emotions. Interestingly, more efficient prefrontal cortex function has also been shown to be associated with higher resting HF (Hansen et al., 2003; Thayer and Brosschot, 2005). Our finding that greater self-
reported use of reappraisal predicted higher resting HRV aligns with these findings. The connections between reappraisal, resting HRV and prefrontal cortex function deserve future empirical investigation in various samples.

4.2 Limitations of the current research

The limitations associated with this research offer additional opportunities for future research. Firstly, as already mentioned, the sample size of this study is relatively small hence no final conclusions can be derived from these preliminary analyses. As this study was cross-sectional in nature, our ability to infer any causal relationships between reappraisal and HRV is limited. Future research should further explore the causal relationships between HRV, ER and psychological wellbeing via longitudinal designs in larger samples. Further, we specifically focussed on two emotion regulation strategies, reappraisal and suppression, due to the extensive research conducted on their relationships with affective symptoms. However, other strategies such as worry/rumination play a major role in the maintenance of anxiety and depression symptoms in non-ASD populations (Yook et al., 2016). Future research should expand the repertoire of ER strategies studied in relation to HRV. Apart from the HRV measure, all other data used in the main analyses, including ASD symptomatology, relied on self-reported measures. The use of multi-informant approach in future studies can minimise this limitation. Finally, it is worth noting that there were five individuals in the control group who scored above the AQ-Short threshold for ASD. This is not surprising given the reported specificity for the AQ-Short is .82 and that ASD traits are thought to be normally distributed in the general population (Hoekstra et al., 2011). In addition, a number of studies have shown significant associations between ASD traits and symptoms of anxiety, depression and
other mental health issues in individuals from the general population (Freeth et al., 2013; Hallett et al., 2012; Rai et al., 2018; Rosbrook & Whittingham, 2010).

4.3 Conclusions

This is the first study to provide preliminary evidence demonstrating the influence of reappraisal use on resting HRV. It is relevant for future longitudinal studies to confirm the direction of causality between reappraisal and HRV in various general and clinical samples. If future research confirms the importance of reappraisal on resting HRV, then this information is useful for informing the design of future interventions. An ER therapy that involves increasing the capacity of individuals to reframe their situation or emotion (i.e., reappraise) has been shown to improve symptoms of affective disorders (Mennin et al., 2015). There is also potential for such interventions to improve autonomic flexibility, however additional work is needed to confirm this hypothesis.
Acknowledgement

Ru Ying Cai acknowledges the financial support of the Cooperative Research Centre for Living with Autism (Autism CRC), established and supported under the Australian Government’s Cooperative Research Centers Program. We would like to thank all those who participated in Ru’s PhD study. We would also like to thank Dr. Emma Baker for coding the ADOS-2 videos as well as Dr. James Heathers and Dr. Mika Tarvainen on their advice on HRV and Kubios, respectively.
References


Table 1. Demographic information

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<td>35.45 (12.19) 19.63 – 56.86</td>
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<td>10 / 10</td>
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* Ethnicity based on the Australian Standard Classification of Cultural and Ethnic Groups
Table 2. Tests of normality results

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<td>.20</td>
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<td>WEMWBS</td>
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<tr>
<td>SDNN</td>
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<tr>
<td>HF</td>
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Abbreviations: AQ, Autism Spectrum Quotient; ERQ-R, Emotion Regulation Questionnaire-Reappraisal; ERQ-S, Emotion Regulation Questionnaire-Suppression; DSM-5 CROSS-D, Diagnostic and Statistical Manual of Mental Disorders-5 Cross-cutting Dimensional Scale; PHQ-9, Patient Health Questionnaire-9; WEMWBS, Warwick-Edinburgh Mental Wellbeing Scale; SDNN, Standard deviation of the NN interval; RMSSD, Square root of the mean squared differences of successive NN intervals; HF, High frequency component.
Table 3. Correlation between key variables

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<th>ERQ-R</th>
<th>ERQ-S</th>
<th>CROSS-D</th>
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Abbreviations: Med., medication; FSIQ, Full Scale Intelligence Quotient; AQ, Autism Spectrum Quotient; ERQ-R, Emotion Regulation Questionnaire-Reappraisal; ERQ-S, Emotion Regulation Questionnaire-Suppression; CROSS-D, Diagnostic and Statistical Manual of Mental Disorders-5 Cross-cutting Dimensional Scale; PHQ-9, Patient Health Questionnaire-9; WEMWBS, Warwick-Edinburgh Mental Wellbeing Scale; SDNN, Standard deviation of the NN interval; RMSSD, Square root of the mean squared differences of successive NN intervals; HF, High frequency component.

* = p < .05
** = p < .01
Figure 1. Histograms of AQ-Short scores for control (blue) and ASD (red)

Abbreviation: AQ, Autism Spectrum Quotient; x axis shows the AQ-Short scores whilst y axis shows the frequency.