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Short communication

High frequency heart-rate variability predicts adolescent depressive symptoms, particularly anhedonia, across one year

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ABSTRACT

Background: Few prospective studies examine the link between lower heart rate variability (HRV) and depression symptoms in adolescents. A recent animal model specifically links HRV to anhedonia, suggesting a potential translational model for human research.
Method: We investigated the association between spectral measures of resting HRV and depressive symptoms measured one year later, among 73 adolescents, aged 11–18 years. We evaluated (1) the predictive power of relative high frequency (HF) HRV, relative low frequency (LF) and relative very low frequency (VLF) HRV for depressive symptoms; and (2) the relative strength of association between HF HRV and depressive symptomatology (anhedonia, negative mood, interpersonal problems, ineffectiveness, negative self-esteem).
Results: HF HRV significantly predicted self-reported depressive symptoms across one year, controlling for age, puberty and sex. HF HRV was most strongly associated with anhedonia one year later, after considering other facets of depressive symptomatology.
Conclusions: Results provide support for the prospective relationship between relative HF HRV and depressive symptoms among adolescents across one year. Findings concur with rodent models that suggest a specific link between HF HRV and anhedonia.
Limitations: We investigated relative spectral power HF HRV and depressive symptom dimensions. We cannot make strong claims about these associations in clinical depression. Physical activity levels could be controlled in future work.

1. Introduction

A growing body of work examines the link between depression and cardiac function, particularly heart-rate variability (HRV) (Carney et al., 2005; Henje Blom et al., 2014; Yaroslavsky et al., 2014). HRV, thought to reflect the impact of the sympathetic and parasympathetic branches of the autonomic nervous system on cardiac function, refers to the measurement of beat-to-beat changes in heart rate (Berntson et al., 1997). While high HRV is associated with healthy cardiac activity—low HRV suggests inadequate parasympathetic or excessive sympathetic activity (Michels et al., 2013; Task Force, 1996). HRV is thought to index the nervous system's impact on the regulation of physiological arousal in proportionate response to an environmental challenge (Appelhans and Luecken, 2006; Thayer and Lane, 2000). HRV is

Abbreviations: HRV, Heart rate variability; HF, High frequency; LF, Low frequency; VLF, Very low frequency; ANS, Autonomic nervous system; RSA, Respiratory Sinus Arrhythmia; MDD, Major Depressive Disorder; HR, Heart rate; ECG, Electrocardiogram; IBI, Inter-beat interval; FFT, Fast Fourier Transform; CDI, Children's Depression Inventory; EATQ DM, Early Adolescent Temperament Questionnaire Depressive Mood Scale; PDS, Pubertal Developmental Scale

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consistently linked to emotion regulation ability—response to stress is associated with HRV reductions (Berntson et al., 1993; Porges et al., 1994), and low resting HRV is associated with negative emotionality and depressive symptoms (Beauchaine, 2001; Thayer and Lane, 2000).

Research investigating the high co-morbidity of adult heart disease and depression found that HRV partially mediated this link (Bhattacharyya et al., 2008; Carney et al., 2005; Celano and Huffman, 2011). Healthy adult studies generally find an association between low HRV and depressive disorders (Gorman and Sloan, 2000; Licht et al., 2008). Similar findings have emerged for youth (Forbes et al., 2006; Shannon et al., 2007; Tonhajzerova et al., 2010). However, demographic factors also need consideration when examining depression-HRV linkages in youth because changes in age and puberty are associated with changes in HRV (Tanaka et al., 2000), and sex might play a role in the link between HRV and depression (Greaves-Lord et al., 2007).

One relevant translational line of research links cardiac function, depression, anhedonia and stress within a rodent model. Depression induced by stress paradigms, (e.g. hindlimb unloading, chronic mild stress) is related to behavioral changes including decreased sucrose intake (a measure of anhedonia) and decreased spontaneous locomotor activity, suggesting reduced appetitive drive (Grippo et al., 2006, 2005; Grippo and Johnson, 2009). Stress-related physiological alterations associated with rodent models of depression include autonomic and cardiovascular changes (e.g. elevated resting heart rate, elevated sympathetic tone, decreased HRV) and immune function changes (e.g. increased pro-inflammatory cytokines, decreased immune response) (Grippo et al., 2003, 2005, 2008; Grippo and Johnson, 2009; Moffitt et al., 2008). This work is particularly relevant because it dovetails with recent human work linking stress, anhedonia, and depression (Pizzagalli et al., 2007).

Few studies examine cardiac activity and depressive symptoms among adolescents prospectively (Yaroslavsky et al., 2014) or discuss HRV and depressive pathophysiology within a translational framework. Our study had two goals. First, we examined HRV at Time 1 [T1] as a predictor of depressive symptoms one year later [Time 2; T2]. Second, we evaluated the relative importance of T2 anhedonia and other depressive symptom facets (negative mood, interpersonal problems, ineffectiveness, negative self-esteem), reflecting the five-factor structure of the Children's Depression Inventory (CDI; Kovacs, 1992), to explain variability in T1 HF HRV.

2. Methods

2.1. Participants

Participants in this report were part of a larger study (Blood et al., 2015), about stress, reward, and risk-taking with 160 typically developing children and adolescents recruited via mass mailings to greater New Haven, CT. Here we report on 73 healthy adolescents (34 boys; *M/SD*=14.82/2.12 years) returning for a one-year follow-up. Participant ethnicities were: 76.7% Caucasian, 9.6% Hispanic or Latino, 6.8% African American, 5.5% Asian, and 1.4% Other. Included participants provided sufficient resting heart rate (HR) data for analysis, were medication free during their electrocardiogram (ECG), and reported no prior history of psychosis, autism, or bipolar disorder. Participants were not excluded based on prior history of depression. Four participants scored at or above the cutpoint for clinical levels of depressive symptoms on the T2 CDI (Costello and Angold, 1988). This research was approved by the Yale School of Medicine Human Investigation Committee.

2.2. Procedure

This study follows up on our previous report that concurrently linked depressive symptoms and HRV (Blood et al., 2015). We recorded participant resting ECG for 7 min. Informed adolescent assent and parental consent were obtained for all participants. Participants received $60 at T1 and $40 at T2.

2.3. Measures

2.3.1. Cardiovascular response

ECG was recorded at T1 using a 3-lead Coulbourn Instruments Holter electrocardiogram, sampled at 1000 Hz, with post processing artifact removal done in QRS tool and spectral analysis done with Kubios software. Three leads were placed – one on the left lower back, one on the right upper back and one on the left arm as a ground. Data processing steps are detailed elsewhere (Blood et al., 2015). Participants with at least six minutes of artifact free data were included (mean 6:57; SD=00:07). Fourier transform (FFT) was used to spectrally analyse IBI data. We extracted three HRV frequency ranges thought to reflect different physiological processes (Shaffer et al., 2014): very low frequency (VLF: .0033–.04 Hz), low frequency (LF: .04–.15 Hz) and high frequency (HF: .15–.4 Hz). Relative power was computed as the percentage of total power in each frequency band (Yeragani et al., 1997).

2.3.2. Depressive symptoms

Adolescents completed the CDI (Kovacs, 1992) at T1 and T2. The CDI contains 27 items scored from 0 to 2. The CDI measures clinical depression and provides a total score and five subscales (anhedonia, negative mood, interpersonal problems, ineffectiveness, negative self-esteem), and was recently replicated in a large sample of children and adolescents (n=4,707) (Garcia et al., 2008).

2.3.3. Pubertal status

Adolescents completed the Pubertal Development Scale (PDS) Self Report and their primary caregiver completed a Parent Report (Petersen et al., 1988) at T1. The 5-item PDS estimates pubertal status based on the presence or absence of developmental features (4-point format). We used the mean of both informants.

2.4. Data analysis

Main study variables included the CDI (T1 and T2), T2 CDI subscales, and T1 spectral power in VLF, LF and HF bands. Analysis included linear regression, (1) using the T2 CDI as the criterion variable with covariates (sex, age, puberty) and T1 HRV spectral relative power measures as predictor variables, (2) then with T1 CDI added to the model, and (3) using T2 CDI subscales to account for variability in T1 HF HRV. Because age, sex, and pubertal status influence HRV, we considered these variables in our correlation and regression analyses.

3. Results

Means and SDs for study variables are presented in Table 1. Correlation analyses (Table 1) revealed that relative T1 and T2 HF HRV was negatively associated with several T2 CDI subscales. T1 LF HRV was positively related to T2 anhedonia, but not related to T2 depression overall. Contrary to our previous report, T1 VLF HRV was not related to T2 depressive symptoms. As expected, sex, age, and pubertal status were significantly associated with HRV (Table 1). We controlled for these variables in our models. Females and males were comparable on depressive symptoms, ($t(71)=-1.48$, $p=.14$).