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# The variable heart: High frequency and very low frequency correlates of depressive symptoms in children and adolescents

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ABSTRACT

Background: Work examining the link between lower heart rate variability (HRV) and depression in children and adolescents is lacking, especially in light of the physiological changes that occur during pubertal development.

Method: We investigated the association between spectral measures of resting HRV and depressive symptoms among 127 children and adolescents, ages 10–17. Using spectral analysis, we evaluated (1) the association between relative high frequency (HF) HRV and depressive symptoms; (2) the predictive power of relative HF HRV for depressive symptoms in the context of relative low frequency (LF) and relative very low frequency (VLF) HRV; and (3) the relationship between relative HF, LF, and VLF band activity, age and pubertal maturation.

Results: Consistent with previous work, results revealed that relative HF HRV was negatively associated with self-reported depressive symptoms. As well, relative VLF HRV was positively associated with depressive symptoms. Regression analyses revealed that relative HF HRV and relative VLF HRV significantly predicted self-report depressive symptoms while controlling for age, sex and pubertal maturation, with relative VLF HRV emerging as the strongest indicator of depressive symptoms. Developmental findings also emerged. Age and pubertal maturation were negatively associated with relative HF HRV and positively correlated with relative VLF HRV.

Conclusions: Results provide support for the relationship between HRV and depression and suggest that both HF and VLF HRV are relevant to depression symptom severity. Findings also reinforce the importance of considering pubertal development when investigating HRV-depression associations in children and adolescents.

Limitations: Influences on cardiac control including physical activity levels and exercise patterns could be controlled in future work. Our data speak to a depressive symptom dimension and relative spectral power HRV. Thus, we cannot make strong claims about relative spectral power HRV and clinical depression.



## 1. Introduction

Depression is a common mental illness, prevalent not only in adults, but also in children and adolescents. According to the National Institute of Mental Health, approximately 11 percent of adolescents have a lifetime prevalence of a depressive disorder, and the risk of developing a depressive disorder increases across adolescence. Interestingly, depressive symptoms in children are strong predictors of later depression in adolescence (Keenan et al., 2009) and also into adulthood (Pine et al., 1999). In addition to its

*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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widely studied cognitive symptoms, depression is associated with a number of physical signs and symptoms including pain, fatigue, digestive problems and even changes in the body's inflammatory response (Bizik et al., 2014; Trivedi, 2004). A growing body of work shows that depression is associated with cardiac function, particularly heart rate variability (HRV) (Carney et al., 2005, 2001), although there is disagreement concerning the cause of HRV abnormalities among those with major depressive disorder (MDD) (Kemp et al., 2011; Licht et al., 2011). Some investigators find that changes in HRV are due to clinical depression itself (Kemp et al., 2010) whereas others report that antidepressant treatment contributes to reductions in HRV (Licht et al., 2010). In their meta-analytic review, Kemp et al. (2010) concluded that among adults without cardiovascular disease, those with MDD had a reduction in HRV (high frequency (HF) spectral measure) and HF HRV was negatively associated with depressive symptom severity. Antidepressant medications did not affect HRV despite clinical improvement in their depressive symptoms, suggesting that the change in HRV is related to the underlying depression, and not medications (Kemp et al., 2010). Conversely, Licht and colleagues (Licht et al., 2010) report a decrease in HRV among individuals with prolonged use of antidepressants, with partially reversible effects after discontinuing the treatment (see Licht et al. (2015) for similar findings older adults). These findings suggest that medications could cause the decrease in HRV, perhaps more than the depression itself (Licht et al., 2010).

HRV is a non-invasive measure of autonomic nervous system (Evans et al., 2013) function. HRV can reflect the balance between the sympathetic and parasympathetic branches of the ANS. The sympathetic nervous system mediates the body's fight or flight response, while the parasympathetic nervous system promotes self-regulation and self-soothing (Porges, 2007). Polyvagal theory links autonomic regulation of the heart to the individual's ability to adapt to challenges in the environment (Porges, 1995b). The ANS, and parasympathetic activity in particular, have been associated with cardiac vagal tone, reflecting input of the vagus nerve to the heart (Porges, 1995c). Vagal control affects the beat-to-beat pattern of the heart, and the amount of variability between heartbeats. HRV is therefore a useful indicator of vagal tone (Friedman, 2007). HRV has been measured by respiratory sinus arrhythmia (RSA), an index of vagal activity that reflects naturally occurring variation in heart rate that occurs during a breathing cycle (Berntson et al., 1997, 1993). Previous work found that low HRV suggests decreased parasympathetic or increased sympathetic activity (Michels et al., 2013; Task Force, 1996). Furthermore, HRV and the related metric, RSA, have been linked to emotion regulation ability across age groups (Berntson et al., 1997, 1993; Porges, 1995a, 1994, 1996). Consistent with the link between vagal tone and emotion regulation (Berntson et al., 1997, 1993; Porges, 1995a, 1994, 1996), low vagal tone at baseline is associated with negative emotional traits (Beauchaine, 2001; Thayer and Lane, 2000). Further, a number of studies in adult samples find an association between low HRV and depressive disorders (Carney et al., 2005; Gorman and Sloan, 2000; Licht et al., 2008; Rechlin et al., 1995, 1994; Roose et al., 1989).

Fewer studies have examined the relation between HRV and depression in adolescents and children. Adolescent studies have focused mainly on females with clinical diagnoses. Henje Blom and colleagues (Henje Blom et al., 2010) found that adolescent females diagnosed with anxiety disorders, major depressive disorder (MDD), or both, had lower HRV compared with healthy controls. In the same study, healthy control participants who reported more depressive symptoms on the Beck Depressive Inventory exhibited less HF HRV (Henje Blom et al., 2010). Similarly, Tonhajzerova et al. (2010) found that female adolescents with MDD showed significantly decreased HRV magnitude compared to a control cohort (Tonhajzerova et al., 2010). Lower RSA has also been linked to MDD in adolescent females (Tonhajzerova et al., 2009). In preadolescents, somatic symptoms were negatively related to HRV, while cognitive symptoms were positively related to HRV (Bosch et al., 2009).

Studies in children more often examine the link between broad-band internalizing problems (spanning anxiety and depression) and HRV. In a study of 3–9-year old children, most with a parent history of child onset depression, low resting RSA was related to internalizing problems (Forbes et al., 2006). Similarly, in a sample of 8–12 year old children at risk for depression and conduct problems, low levels of RSA conferred significant risk for depression (Shannon et al., 2007). Dietrich and colleagues (2007) found that low basal RSA predicted internalizing symptoms in children (Dietrich et al., 2007), while Hinnant and El-Sheikh (2009) observed that lower levels of basal RSA predicted both internalizing and externalizing symptoms, although under stress greater internalizing symptoms predicted RSA suppression whereas greater externalizing symptoms predicted RSA augmentation (Hinnant and El-Sheikh, 2009). Taken together, these studies suggest lower basal RSA or RSA "at rest" is associated with greater depressive and internalizing symptomatology in children and adolescents.

Much of the previous work has used RSA as an index of HRV (Berntson et al., 1997, 1993). The overall variability that composes HRV can also be broken down into the frequency components. Frequency domain analysis involves taking heart rate inter beat interval measures and computing a spectral analysis with the Fourier transform, with multi-second frequency bands (high, low, and very low) serving as indices of HRV (Akselrod et al., 1981). Spectral analysis allows for the examination of the level and type of rhythmic activity of underlying physiological systems that support cardiac flexibility. From this perspective, high frequency (HF) HRV has been used as an index of parasympathetic activity. RSA corresponds to the respiratory frequency, 0.15–0.4 Hz, equivalent to the HF band range. Low frequency (LF: 0.04–0.15 Hz) HRV is thought to reflect both sympathetic and parasympathetic effects on HRV (Berntson et al., 1997; Silva et al., 2009). Less is known about the controlling factors of very low frequency (VLF: 0.0033–0.04 Hz) HRV. Some studies suggest a relationship with humoral factors such as thermoregulation and the renin-angiotensin system (Bernardi et al., 1996; Lindqvist et al., 1990; Taylor et al., 1998), while others consider temperature, metabolic and hormonal influences (Friedman, 2007).

Relatively few studies employ spectral analysis to examine the relationship between HRV and depression in adolescents and children. For instance, Tonhajzerova and colleagues (2009) found that female adolescent participants with MDD had significantly less HF HRV compared to healthy matched subjects (Tonhajzerova et al., 2012). At the same time, some recent work reports links between VLF and treatment outcomes in patients with MDD (Jain et al., 2014). Results indicate that lower baseline relative power of VLF predicted improvement in depressive symptoms. Greater relative power of VLF has also been connected with higher depression severity in depressed patients (Davydov et al., 2007). These results suggest VLF may also be a potential correlate of depressive pathophysiology.

Importantly, developmental factors need attention when considering individual differences in HRV among children and adolescents and HRV as a correlate of depressive pathophysiology. The onset of pubertal maturation is a time for changes in stress responsiveness and emotional reactivity that connect to a heightened risk for psychopathology during adolescence (Dahl and Gunnar, 2009; Evans et al., 2013; Stroud et al., 2009; Van den Bos et al., 2014). An association between depression and pubertal status has been documented (Joinson et al., 2012). As well, starting