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Heart Rate Variability in Depression: Effect of Escitalopram

Angelos Halaris, MD; John Piletz, PhD; Erin Tobin, MA;
Edwin Meresh, MD; James Sinacore, PhD; and Christopher Lowden

Department of Psychiatry, Loyola University Chicago Stritch School of Medicine,
Maywood, IL

There is high bidirectional comorbidity between depression and cardiovascular morbidity and mortality. Depression has been associated with a higher risk for myocardial infarction even after controlling for hypertension, dyslipidemia, obesity, smoking, and physical inactivity. Altered autonomic tone in depression with sustained sympathetic overdrive and diminished vagal tone leads to pervasive loss of homeostasis, referred to as allostatic load. Such an allostatic load is a likely contributor to the increased risk of mortality in patients with depression. Measuring heart rate variability (HRV) is an accepted method for assessing cardiac autonomic tone and a measure of allostatic load. Depression has been associated with decreased HRV in otherwise physically healthy patients, although not all studies agree. HRV can be determined on the basis of frequency and time domains. High-frequency (HF) measures reflect parasympathetic activity, while low-frequency (LF) measures reflect mainly, but not exclusively, sympathetic activity. A ratio of LF/HF is calculated to determine the degree of homeostatic imbalance.

Of interest is whether the allostatic load of depression is reversible with antidepressant interventions and whether cardiac health is restored when the depressed mood is successfully treated. Previous studies using pharmacological treatments of depression have suggested that the allostatic load defined by diminished HRV in depression is not reversed after 4 to 16 weeks on various antidepressants. Some studies suggest that antidepressants,

probably due to anticholinergic- and/or noradrenergic-enhancing properties, aggravate the already reduced HRV (Licht et al, 2008; Van Zyl et al, 2008). We undertook this study to (a) reassess the effect of depression on HRV, and (b) assess the ability of escitalopram (ESC), the most selective of the selective serotonin reuptake inhibitors available on the market, to restore HRV.

We report initial findings of HRV at rest in 17 patients with major depression (MDD) and 6 healthy controls. Eleven of the patients were evaluated again after 12 weeks of ESC treatment. Supine HRV recordings (10 min) were analyzed to distinguish LF and HF domains. Prior to treatment, most of the MDD patients (12/17) had > 50% LF variability, indicative of sympathetic overdrive, but there was overall no statistical difference from controls in any HRV parameter. Following 12 weeks of ESC treatment ($n = 11$), there was overall a highly significant ($P = 0.006$) normalization toward a 50%:50% LF/HF ratio, which is considered to be normal for a short rest. This move toward 50:50 was observed whether the patients started in sympathetic excess (> 50% LF) or parasympathetic excess (> 50% HF).

A logistic regression analysis was conducted using age, sex, ethnicity, HAM-D (severity of depression), HAM-A (severity of anxiety), and an insomnia scale to identify those patients whose HRV ratio increased ($N = 4$) or decreased ($N = 7$) after treatment. No predictors were significant, but the pretreatment HAM-A score was marginally significant ($P = 0.065$). This finding suggests that the extent of anxiety symptoms in depressed patients sometimes results in sympathetic overdrive but that, regardless of pretreatment anxiety, all patients tended to achieve a 50:50 balance in the HRV frequency domains after 12 weeks of treatment with ESC. ESC may be advantageous for restoring cardiac health since other pharmacological agents have not been found to affect HRV favorably in depression.

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