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Distinguishing bipolar from unipolar disorders on the basis of heart rate variability

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To the Editor,

Heart rate variability (HRV) provides an important marker of vagal function that may underpin established links between mental and physical health (Kemp and Quintana 2013). For this reason I was interested to read the recent article by Hsin-an Chang and colleagues (Chang et al. 2015) on the differences in HRV between patients with bipolar II (BPII) depression and unipolar major depressive disorder, relative to healthy controls. While this study has a number of strengths – including a large sample size and attention to confounding variables – I strongly disagree with their conclusion that "HRV may aid in differential diagnosis" on the basis of the presented data.

Firstly, Chang concludes that patients with BPII display sympathetic nervous system activation (SNS) (indexed by higher LF/HF ratio) and reciprocal vagal impairment, while those with UD only display vagal impairment. However, these conclusions are unwarranted, because measures of HRV – including the LF-HRV component – are determined primarily by the parasympathetic system (see Reyes Del Paso et al. 2013 for discussion). The extent to which HRV taps into the sympathetic nervous system has been a topic of considerable debate over recent years (see also Goldstein et al. 2011 for review). Regardless, it is most unlikely that the LF/HF ratio extracted from resting-state conditions will reflect sympathovagal balance.

Secondly, the authors did not refer to several recent studies of ours, which make an important contribution to the discussion over the impact of UD on HRV, the impact of confounding variables, and disorder heterogeneity. Last year we published one of the largest studies to date that controlled for confounders using an under-used propensity score matching (PSM) technique (Kemp, Brunoni, et al. 2014). We reported that patients with generalized anxiety disorder, but not major depression disorder (MDD), display robust decreases in HRV after PSM. However, in a follow-up study (Kemp, Quintana, et al. 2014) on an independent cohort, we reported that MDD patients with

melancholia – but not those with non-melancholia – display HRV decreases relative to controls, findings associated with a moderate effect size. It is relevant here that the large UD group in Chang's study was comprised of 130 patients with melancholic features, yet the extent to which these participants differ from those with BPII was not examined in their study.

In conclusion, while I commend the authors' contribution to this important field of research, I remain unconvinced by the argument that BPII differs from UD on HRV measures. The LF/HF ratio is unlikely to be a measure of SNS activity during resting-state conditions and I query the extent to which groups would differ on other HRV measures if a more homogeneous group of UD patients – such as those with melancholic features – were to be compared with BPII patients. Finally, this letter provides an important opportunity to flag the problems associated with null hypothesis significance testing and the need for 'the new statistics' (Cumming 2014) to be integrated into HRV studies when examining the extent and clinical relevance of observed differences across psychiatric disorders.

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