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Resting state vagal tone in borderline personality disorder: A meta-analysis

Julian Koenig [a,b,*], Andrew H. Kemp [c,d], Nicole R. Feeling [b], Julian F. Thayer [b,1], Michael Kaess [a,1]

[a] Department of Child and Adolescent Psychiatry, Centre for Psychosocial Medicine, University of Heidelberg, Heidelberg, Germany
[b] The Ohio State University, Department of Psychology, Columbus, OH, USA
[c] University Hospital and Faculty of Medicine, University of São Paulo, São Paulo, Brazil
[d] School of Psychology & Discipline of Psychiatry, University of Sydney, Sydney, Australia

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ABSTRACT

Borderline personality disorder (BPD) is the most common personality disorder in clinical settings. It is characterized by negative affectivity, emotional liability, anxiety, depression, as well as disinhibition (i.e., impulsivity and risk taking), all of which have been linked to lower resting state vagal tone, which may be indexed by vagally-mediated heart rate variability (vmHRV). Here, we aimed to quantify the current evidence on alterations in resting state vmHRV in individuals with BPD, relative to healthy controls. A rigorous search of the literature, according to the "*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*", revealed 5 studies suitable for meta-analysis, reporting vmHRV in individuals with BPD ($n = 128$), relative to healthy controls ($n = 143$). Short-term measures of resting state vmHRV were extracted and subjected to meta-analysis using both random- and fixed effect models in *RevMan*. BPD displayed lower resting state vmHRV relative to healthy controls in random- (Hedges' $g = -0.57$, 95% CI [−1.12; −0.01], $k = 5$) and fixed-effect meta-analysis (Hedges' $g = -0.54$, 95% CI [−0.84; −0.25], $k = 5$). Control for potential publication bias did not change observed findings. Lowered resting state vagal tone may be an important trait characteristic underlying BPD. As prior studies have observed lowered vmHRV in a variety of psychiatric disorders, we propose that lowered vmHRV may reflect a common psychophysiological mechanism underlying difficulties in emotion regulation and impulsivity, in particular.

1. Introduction

Borderline personality disorder (BPD) is characterized by pathological personality traits in the domains of negative affectivity, emotional liability, anxiousness, separation insecurity or depressivity and behavioral characteristics such as disinhibition (i.e., impulsivity and risk taking) and antagonism (hostility) (American Psychiatric Association, 2013; Leichsenring et al., 2011). BPD affects about 1–2% (Coid et al., 2006; Trull et al., 2010) of the general population and is the most common personality disorder in clinical settings (American Psychiatric Association, 2001).

Several key features of BPD (i.e., emotional liability and impulsivity) represent impairment in inhibitory control, the capacity to inhibit and regulate prepotent emotional responses. Heart rate variability (HRV) – the variability in the time-series of consecutive heartbeats – is widely perceived as a psychophysiological marker of emotion regulation capacity (Lane et al., 2009; Park and Thayer, 2014) and inhibitory control (Gillie et al., 2014; Hovland et al., 2012; Pappens et al., 2014; Wendt et al., 2015). Parasympathetic modulation of the heart rate is fast (timescale on the order of milliseconds) while sympathetic effects are much slower (Levy, 1997). Therefore, high-frequency (HF) HRV, respiratory sinus arrhythmia (RSA), and time-domain measures reflecting these fast changes (i.e., the time-domain root-mean-square of successive R–R-interval differences, RMSSD measure) provide a readily available, surrogate measure of vagal activity (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Vagally mediated HRV (vmHRV) is strongly associated with emotion regulation (Thayer et al., 2012) and underpins individual differences in the perception of emotional stimuli (Park et al., 2013). It predicts affective instability in daily life (Koval et al., 2013) and is inversely correlated to greater reports of difficulties in emotion regulation (Berna et al., 2014; Williams et al., 2015). While emotional dysregulation is a core feature of BPD itself, it may also be an important candidate to explain high rates of comorbidity between BPD and other mental disorders (e.g. substance use disorders and affective disorders) (Dell'Osso et al., 2010).

Furthermore, lower vmHRV has been linked to a variety of other mental and physical health conditions (Kemp and Quintana, 2013),

* Corresponding author at: University of Heidelberg, Department of Child and Adolescent Psychiatry, Centre for Psychosocial Medicine, Blumenstrasse 8, 69115 Heidelberg, Germany.
E-mail address: Julian.Koenig@med.uni-heidelberg.de (J. Koenig).
[1] Equally contributing senior authors.

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within the psychiatric domain in particular (Malik and Camm, 2007). Reduced vmHRV relative to controls is reported in major depressive disorder (MDD) (Kemp et al., 2010) and MDD with comorbid generalized anxiety disorder (Kemp et al., 2012), as well as MDD with melancholia (Kemp et al., 2014a, 2014b). Reduced vmHRV is also observed in anxiety disorders (Chalmers et al., 2014) such as social anxiety disorder (Alvares et al., 2013), generalized anxiety disorder (Friedman and Thayer, 1998a; Thayer et al., 1996, 2000), and panic disorder (Cohen et al., 2000; Friedman and Thayer, 1998b). Intriguingly, HRV has also been linked to risk taking behavior (Bhatt et al., 2015) as well as to personality traits (e.g. neuroticism) in the general population (Čukić and Bates, 2014; Huang et al., 2013; Zohar et al., 2013) and interpersonal dysfunction (Hansen et al., 2007).

Given the associations and commonalities of key-features of BPD and vmHRV, vagal tone is a promising target for research into shared mechanisms underlying psychopathological disorders that are sequentially comorbid (Caspi et al., 2014) and manifest as BPD. Here we aimed to review and quantify the current evidence on differences in resting state vagal tone comparing individuals with BPD and healthy controls.

2. Methods

2.1. Literature search

A systematic search of the literature, according to the "*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*" (PRISMA) statement (Moher et al., 2009) was employed using the *PubMed*, *PsycNET/PsycINFO*, *CINAHL Plus*, and *Web of Science* (WOS) databases (see Appendix A for search terms and hits by database). Additionally, a hand search (i.e., *Google*, *Google Scholar* and other sources) was performed and reference lists of included studies were checked for additional studies eligible for inclusion. After removing duplicates, abstracts of all articles were screened based on pre-defined inclusion criteria. Abstracts were included if they reported (i) *an empirical investigation* in (ii) *humans* and (iii) *recorded HRV* (iv) *in BPD*. All titles meeting the inclusion criteria were retrieved and reviewed in full-text. Excluded studies and reasons for exclusion are given in Fig. 1. Empirical investigations were defined as studies involving active data collection in human subjects. Reviews, meta-analysis, comments, single-case reports, or abstracts from conference proceedings were excluded. The full-text of studies qualifying for inclusion were further reviewed and screened for inclusion eligibility. To be included, studies had to report (i) *any measure of vmHRV* in (ii) *clinical samples of BPD patients* characterized by clinical criteria (e.g. DSM, ICD) and diagnostic procedures, or (iii) individuals *high on borderline personality features*, as assessed by psychometric instruments with high specificity and sensitivity when compared to a validated structured clinical interviews; compared to (iii) *non-BPD healthy controls*.

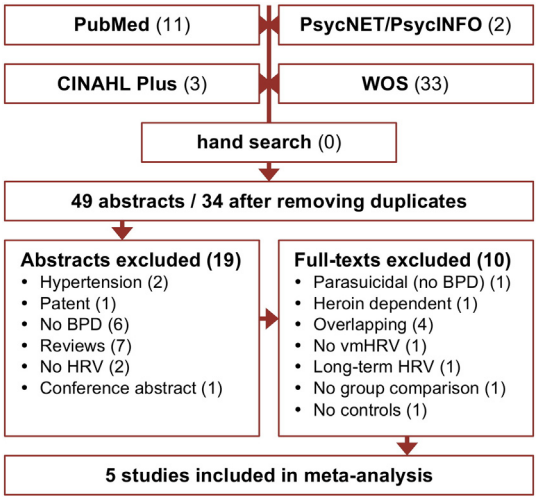

Fig. 1. PRISMA flow-chart.

2.2. Data extraction

All time- and frequency domain measures reflecting vmHRV were considered for inclusion in the meta-analysis. Where citations reported multiple indices of vmHRV, hierarchical inclusion criteria were implemented to prevent conflation of effect-size estimates: HF power was selected for analysis if available, followed by RSA and RMSSD. Authors who reported vmHRV but who did not provide sufficient quantitative data (e.g., only a graphical display) were contacted in order to request the necessary information to derive effect size estimates and confidence limits on the selected indices. When only the standard error of the mean (SEM) was reported, the SD was calculated by multiplying the SEM by the square root of the sample size (Higgins and Green, 2011). When descriptive statistics were reported other than the mean, SD or SEM, data were imputed by established procedures where possible (Glass et al., 1981; Wiebe et al., 2006). Studies that reported more than two groups of participants (e.g. BPD vs. generalized anxiety disorder vs. healthy controls) were included as long as findings were available from at least one BPD group against healthy controls, while studies that compared different groups of BPD patients only were excluded. When multiple groups of BPD patients (e.g., BPD with and without avoidant personality disorder) were reported, each group was compared to the same group of healthy controls.

Descriptive statistics (mean and SD) of vmHRV indices derived from resting baseline recordings were extracted. Where longitudinal or pre-post data were reported, only baseline resting HRV was included to minimize confounding effects by experimental manipulation and conflation of effect size estimates. If long-term (e.g. 24 h) recordings were obtained, measures from these recordings were included in the analysis. However, it is noted that guidelines for the measurement of HRV suggest "*because of the important differences in the interpretation of the results, the spectral analyses of short- and long-term electrocardiograms should always be strictly distinguished*" (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Thus, meta-analysis for short- and long-term recordings was done separately when sufficient data was available for analysis.

2.2.1. Effect estimation and heterogeneity

True effect estimates were computed as adjusted standardized mean differences (Hedges' g). Meta-analyses were performed using both fixed-effect (FE) and random-effects (RE) models. When results of both analyses were consistent (with confidence intervals (CI) of fixed-effect analyses being included within that of the random-effects analysis), the results from random-effects models are reported and graphically displayed, as it better conveys the variability of data (Higgins and Green, 2011). Possible sources of heterogeneity or inconsistency among trials in the magnitude or direction of effects were investigated. Bias was examined using a funnel plot of effect size against standard error for asymmetry and heterogeneity was assessed using the standard I^2 index, Chi-square, and Tau^2 tests (Higgins and Thompson, 2002). Substantial heterogeneity was assumed if I^2 was greater than 50%, indicating that 50% of the variability in the outcome cannot be explained by sampling variation. Meta-analytic computations were performed using *RevMan* (*Version 5.3.4, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014*).