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Short communication

Nonverbal behaviors are associated with increased vagal activity in major depressive disorder: Implications for the polyvagal theory

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A R T I C L E I N F O

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A B S T R A C T

Background: Major depressive disorder (MDD) is associated with impairments in nonverbal behaviors (NVBs) and vagal activity. The polyvagal theory proposes that vagal activity regulates heart rate and NVBs by modulating a common anatomically and neurophysiologically discrete social engagement system. However, the association between these putative endophenotypes has not yet been explored. We hypothesize that in MDD, NVBs indicating positive affects and social interest and those indicating negative feelings and social disinterest could be associated with different patterns of vagal activity.
Methods: For this cross-sectional study we recruited 50 antidepressant-free participants with moderate-to-severe MDD. Vagal activity was indexed by heart rate variability (HRV) measures, and positive and negative nonverbal behaviors (NVBs) by a validated ethogram. Associations between NVBs and HRV were explored by bivariate analyses and multivariable models were adjusted by age, gender, depression severity, and self-reported positive and negative affects.
Results: HRV measures indicative of higher vagal activity were positively correlated with positive NVBs exhibited during the clinical interview. Conversely, NVBs related to negative affects, low energy and social disinterest were not associated with HRV.
Limitations: Absence of a control group.
Conclusions: The findings highlight that the examined depression endophenotypes (nonverbal behaviors and vagal activity) are related, shedding light on MDD pathophysiology in the context of the polyvagal theory.

1. Introduction

Several studies have investigated the role of nonverbal behaviors (NVBs) in social functioning in major depressive disorder (MDD). For instance, decreased facial and head movements are related to depression severity (Fiquer et al., 2013; Girard et al., 2014), and behavioral patterns can aid in differentiating depression from other psychiatric disorders in patients (Annen et al., 2012). Depression improvement is also associated with an increase in social interest behaviors (Fiquer et al., 2013; Girard et al., 2014).

NVBs are controlled not only by the central, but also by the autonomic nervous system (ANS) (Appelhans and Luecken, 2008). According to the polyvagal theory (Porges, 2011), vagal motor pathways regulating heart rate and head striated muscles are anatomically and neurophysiologically part of the same system that induces complex adaptive and emotional responses. Consequently, the social engagement system, which regulates social behavior and communication, is linked to the myelinated vagus, and can only function efficiently when

Abbreviations: MDD, major depressive disorder; NVB, nonverbal behavior; HRV, heart rate variability; HF, high frequency; LF, low frequency; HDRS, Hamilton Depression Rating Scale; RMSSD, root mean squares of successive differences; PANAS, Positive and Negative Affect Schedule

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defensive circuits (such as the "fight or flight" response) are inhibited (Porges, 2011).

Hence, the inhibitory role of cortical structures is critical for downregulating vagal activity (Thayer et al., 2009). This might explain why disorders associated with prefrontal dysfunction, such as MDD, are associated with a reduction of vagal activity reflected by decreased heart rate variability (HRV) (Kemp et al., 2014). In fact, HRV is determined by a variety of physiological factors, particularly the ANS. In the resting state, the heart is under tonic inhibitory control by the parasympathetic (vagal) nervous system, whereas heart rate increases during increased sympathetic input on the sinoatrial node. (Kikuchi et al., 2009). In this context we refer to HRV as surrogate marker of ANS activity.

However, although patients with MDD present alterations in NVBs and vagal activity, the relationship between these has not yet been explored – and consequently was the aim of the present study. Our a priori hypothesis was that "positive" behaviors (i.e., nonverbal indicators of social interest, positive feelings and/or willingness to communicate) would be associated with higher vagal activity, whereas "negative" behaviors (i.e., nonverbal indicators of social disinterest, low energy and/or negative feelings) would be associated with lower vagal activity. This investigation may provide a better understanding of the role of the ANS in the pathophysiology of MDD in the context of polyvagal theory.

2. Methods

2.1. Study design

This cross-sectional study used ECG recordings and a previously validated ethogram, respectively, to evaluate HRV and NVBs. Patients were recruited from an ongoing clinical trial (Brunoni et al., 2015). The local and national Ethics Committee approved this study and all participants provided written informed consent. This study is in accordance with a recently published guideline on reporting psychiatric studies using HRV (Quintana et al., 2016).

2.2. Subjects

Participants were recruited by media advertisements and physician referrals. They were pre-screened in brief telephone and e-mail interviews, and those meeting the general criteria underwent additional onsite screening (Supplementary material).

2.3. Procedure

Prior to randomization or any intervention, HRV and NVBs were assessed. In most cases, HRV was collected immediately after the NVB assessment, although in some cases HRV was only collected the next day for logistical reasons.

2.3.1. Heart rate variability (HRV)

HRV is an ECG-based technique characterized by the examination of periodic and non-periodic oscillations of heartbeats which can be detected by changes in the length of the R–R intervals. Spectral analysis of the ECG distinguishes high (HF) and low (LF) frequency bands. HF is mainly associated with vagal activity, and LF with parasympathetic and sympathetic activity. Another HRV index is the root mean squares of successive differences (RMSSD), which is also associated with vagal activity. HRV procedures are described in the Supplementary Material.

2.3.2. Behavioral assessment

Behavioral assessment was performed during a 15-min interview by a trained psychologist (JTF). Patients were asked to describe their daily routine, current events, and mood state while being filmed. The camera was adjusted to record each patient's face and trunk. The footage was used to analyze patients' behavior, using ten 30 s sequences of time during the first 5 min of the interview. Two trained raters who were blinded to the study objectives recorded the presence (score 1) or absence (score 0) of 20 behavioral categories at each period of time, using a standardized ethogram (Fiquer et al., 2013) developed specifically to assess the behaviors patients exhibited during recorded clinical interviews. Raters performed at a uniform level of inter- and intra-rater reliability (kappa scores of 0.76 and 0.85, respectively). From the 20 behavioral categories, 10 are associated with positive affects and/or favorable disposition to social contact ("positive behaviors"), and 10 are associated with negative affects, low energy and/or social disinterest ("negative behaviors").

2.3.3. Clinical scales

Patients were also evaluated by the Portuguese-validated versions of the Positive and Negative Affect Schedule (PANAS), State-Trait Anxiety Inventory (STAI) and HDRS-17 (Gorenstein and Andrade, 1996).

2.4. Statistical analysis

Analyses were conducted with Stata 12 software (Statacorp, College Station, TX, USA), and the sample was described by means and frequencies. The Shapiro-Wilk and Levene tests were used to check the normality and homoscedasticity of data, respectively. In all the analyses, results were significant at $p \leq 0.05$.

Spearman's Rho test was used to evaluate associations between HRV variables, computed total scores of positive and negative NVBs, and continuous data relevant for our analyses such as age, depression severity (HDRS-17), duration of the current depressive episode, body mass index, number of previous depressive episodes, and scores from the Positive and Negative Affects Scale (PANAS) and the State-Trait Anxiety Inventory (STAI). T-tests were used to explore the influence of categorical variables such as gender, physical activity, social drinking, smoking status, hypertension, and use of benzodiazepines on HRV and NVB. Physical activity was assessed using the IPAQ questionnaire (Craig et al., 2003) and was categorized as inactive vs. active. "Social drinking" was defined as a drinking habit in social gatherings without the intention to get drunk or other patterns related to excessive alcohol use (binge drinking, heavy drinking). Importantly, participants presenting diagnoses of alcohol abuse or alcohol dependence were not included according to our eligibility criteria.

Univariate linear regression models were initially performed to further investigate the association between HRV and NVBs. The first step was to perform a natural logarithmic transformation of HRV measures to ensure data normalization. Next, HRV variables were introduced as outcome variables in our model and NVBs as predictors.

Subsequently we constructed multivariate linear regression models. Here we used a forced-entry method in which covariates were introduced based on clinical reasoning rather than testing the collected covariates. We did this because of the high number of available variables (since multiple testing could inflate type I error) and the relatively low number of observations (n=50), which meant that introducing several predictors would lead to underpowered analyses, increasing type II error. The covariates age and gender were selected for their high influence on HRV measures and baseline depression and PANAS because of its possible influence on NVB measures. Finally, anxiety-trait and anxiety-state were assessed due to their influence on both HRV and NVB measures.

3. Results

Participants were recruited between February and July 2014. During this period, 130 volunteers were interviewed and 80 were excluded due to: depression of low/mild intensity (n=28), use of