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Research report

Relationship between cardiac vagal activity and mood congruent memory bias in major depression

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ABSTRACT

Background: Previous studies suggest that autonomic reactivity during encoding of emotional information could modulate the neural processes mediating mood-congruent memory. In this study, we use a point-process model to determine dynamic autonomic tone in response to negative emotions and its influence on long-term memory of major depressed subjects.
Methods: Forty-eight patients with major depression and 48 healthy controls were randomly assigned to either neutral or emotionally arousing audiovisual stimuli. An adaptive point-process algorithm was applied to compute instantaneous estimates of the spectral components of heart rate variability [Low frequency (LF), 0.04–0.15 Hz; High frequency (HF), 0.15–0.4 Hz]. Three days later subjects were submitted to a recall test.
Results: A significant increase in HF power was observed in depressed subjects in response to the emotionally arousing stimulus ($p=0.03$). The results of a multivariate analysis revealed that the HF power during the emotional segment of the stimulus was independently associated with the score of the recall test in depressed subjects, after adjusting for age, gender and educational level (Coef. 0.003, 95%CI, 0.0009–0.005, $p=0.008$).
Limitations: These results could only be interpreted as responses to elicitation of specific negative emotions, the relationship between HF changes and encoding/recall of positive stimuli should be further examined.
Conclusions: Alterations on parasympathetic response to emotion are involved in the mood-congruent cognitive bias observed in major depression. These findings are clinically relevant because it could constitute the mechanism by which depressed patients maintain maladaptive patterns of negative information processing that trigger and sustain depressed mood.

1. Introduction

Emotional events are preferentially encoded in mood states with a matching affective valence (Holland and Kensinger, 2010). For instance, a happy mood enhances retrieval of memories with positive attributes, while negative memories predominate in sad moods. This phenomenon is the basis for the negative bias in episodic memory observed in subjects with Major Depression (MD) (Matt et al., 1992).

The neurobiological mechanisms mediating the facilitation effects of emotion on episodic memory are only partly understood. Nevertheless, some studies have pointed out that activation of the autonomic nervous system (ANS) during encoding or retrieval of emotional information could modulate the neural processes mediating mood congruent memory (Critchley et al., 2013). Mood disorders have been previously associated with alterations in ANS functioning (García-Gómez et al., 2007). Depressed subjects frequently present clinical symptoms related with autonomic

Abbreviations: ANS, autonomic nervous system; ECG, electrocardiogram; HC, healthy control; HF, high frequency; HRV, heart rate variability; KS, Kolmogorov-Smirnov; LF, low frequency; MAD, median absolute deviation; MD, major depression.

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Table 1
Narrative accompanying the slide presentation.

Slide	Neutral version	Emotional version
1.	A mother and her son are leaving home in the morning.	A mother and her son are leaving home in the morning.
2.	She is taking him to visit his father's workplace	She is taking him to visit his father's workplace
3.	The father is the chief laboratory technician at a nearby hospital.	The father is the chief laboratory technician at a nearby hospital.
4.	They check before crossing a busy road.	They check before crossing a busy road.
5.	While walking alone, the pass the scene of a minor accident, which the boy finds interesting.	While crossing the road, the boy is struck by a runway car, which critically injures him.
6.	At the hospital, the staff are preparing for a practice disaster drill, which the boy will watch.	At the hospital, the staff prepare the emergency room, to which the boy is rushed.
7.	All morning long, surgeons practiced the standard drill procedures.	All morning long, surgeons struggled to save the boy's life.
8.	Special make-up artist were able to create realistic injuries on actors for the drill.	Specialized surgeons were able to succesfully re-atach the boy's severed feet.
9.	After the drill, while the father stayed with the boy, the mother left to phone her other child's preeschool.	After the surgery, while the father stayed with the boy, the mother left to phone her other child's preschool.
10.	Running late, she phones the preschool to tell them she will soon pick up her child.	Feeling distraught, she phones the preschool to tell them she will soon pick up her child.
11.	Heading to pick up her child, she hails a taxi at the number nine bus stop.	Heading to pick up her child, she hails a taxi at the number nine bus stop.

dysfunction such as sleep pattern alterations, decreased appetite, gastrointestinal paresthesia and increased sweating (Tylee and Gandhi, 2005). In addition, multiple studies have reported decreased heart rate variability (HRV) and baroreflex sensitivity in these subjects (Kemp et al., 2010; Garcia et al., 2012). We hypothesize that in response to emotions with a negative valence, such as sadness or disgust, depressed subjects present alterations in ANS reactivity which could be one of the mechanisms for the increased encoding of negative events and the persistence of rumination associated to MD.

Since the ANS responds to emotional stimuli with rapid time-varying dynamics, computational tools able to discern these changes with high time resolution are the best candidates for providing optimal assessments. Standard HRV analysis does not comply with this requirement since it requires relatively long-time intervals (minutes) of electrocardiogram (ECG) acquisitions and is unable to detect rapid variations (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). To overcome these limitations, we propose the use of an effective statistical computational tool for the analysis of HRV series, based on the so-called point-process theory (Barbieri et al., 2005). Such a point-process analysis, in fact, represents a pioneering study in the field of mood assessment, as just being recently proposed for the characterization of heartbeat dynamics in patients with mood disorders (Valenza et al., 2014, 2015a, 2015b). The core of the model is the definition of the inter-heartbeat probability functions to predict the waiting time of the next heartbeat, i.e. the R-wave event, given a linear combination of the previous heartbeat events. In addition, the point-process model can be applied without using any prior interpolation method which might bias the HRV analysis (Barbieri et al., 2005). Finally, the model parameters are personalized and defined in an instantaneous fashion, and validated through a proper goodness of fit analysis (Barbieri et al., 2005).

In this study, we use this HRV point-process model to determine the relationship of dynamical vagal tone, as estimated through the instantaneous high frequency (HF) power, in response to negative emotions with the ability to encode and retrieve this information in depressed subjects compared to healthy controls.

2. Methods

2.1. Subjects

Forty-eight Hispanic outpatients with MD (age: 22.6 ± 4.7 years) were included in the study. All subjects were screened from local universities by applying the Zung-self-rating depression scale (Zung, 1965). This scale is a 20-item questionnaire that measures the presence and severity of depressive symptomatology during the preceding two weeks. A score of 50/100 was considered compatible with a diagnosis of depression according to previous data in our population (Campo-Arias et al., 2006). A Spanish Structured Clinical Interview for DSM-IV Axis I disorders, Clinical version, was applied by qualified psychiatrists to confirm the MD diagnosis. All patients were experiencing their first depressive episode and had not received psychotherapeutic or pharmacological treatment. A control group consisting in 48 age- and gender-matched healthy control (HC) subjects was also included (age: 23.5 ± 4.9 years). Sixteen men (33.3%) and 32 women (66.6%) were included in each group. Exclusion criteria for both MD and HC subjects were known cardio-, cerebro-, or peripheral vascular disease, presence of neoplasm, diabetes mellitus, kidney or liver failure, infectious or systemic inflammatory disease and current neurological illness. All subjects received information about the study procedures and gave written informed consent approved by an Institutional Review Board.

2.2. Stimulus material

The stimulus used in the study consisted on a set of eleven slides accompanied by a narrative with two different versions: one emotionally neutral (N) and the other emotionally arousing (E). These stories had been previously adapted and validated in a Colombian sample (Oliveira et al., 2004) and were kept as close as possible to the originals (Cahill and McGaugh, 1995). Both set of slides show a mother taking her young son to see his father at a nearby hospital where he works. In the N version of the story, the mother and son witness a minor car accident, which attracts the attention of the child, whereas in the E version the child himself is critically injured and requires a surgical intervention at the hospital. The story's content can be divided into three phases, with the second period (slides 5–8) comprising the emotionally arousing elements (table 1). At the end of the presentation, each subject was asked to rank the story according to the emotional content (0 to 10, in which 0 corresponded to “not emotional” and 10 to “highly emotional”).

2.3. Procedures and recording of physiological variables

All recording sessions took place between 8 a.m. and 10 a.m. All tests were performed in a quiet, dimly lit room at a comfortable temperature (20–22 °C). Participants abstained from smoking or consuming beverages containing caffeine, xanthines or alcohol the