A model of neurovisceral integration: the central-autonomic network in psychopathology and medical conditions

ABSTRACT: Autonomic nervous system (ANS) dysregulation, mostly a reduced cardiac vagal tone as measured by the high frequency (HF) power of heart rate variability (HRV), is a key factor in psychopathology, including depression, severe mental illness (SMI) [1], as well as several medical conditions (e.g., cardiovascular disease) [2]. A network of brain regions (the central autonomic network; CAN) – including the anterior cingulate (ACC), insular, orbitofrontal, and ventromedial prefrontal cortices, and the amygdala – has been shown to be affected in psychopathology, mostly when associated with somatic symptoms. Through projections to the hypothalamic and brainstem autonomic nuclei, this network has been also postulated to control HRV. Studies using neuroimaging techniques and EEG co-registration, proposed a key role of theta activity linking CAN, particularly rostral ACC activity, to HRV.

Project_1 **The central-autonomic network in the association between depression and coronary heart disease (CHD) (PI: Palomba; co-PIs: Ponchia[1](external), Bertoldo, Gentili, Messerotti Benvenuti)**

Over the last 10 years, depression has emerged as a risk factor for mortality in patients recovering from myocardial infarction (MI), where clinical depression is associated with a 2- to 4-fold increase in mortality. ANS has been identified as a pivotal site of dysregulation, with reduced parasympathetic (PSNS) and increased sympathetic (SNS) nervous system activity leading to arrhythmias and sudden cardiac death. The presence of depression may potentiate the impaired ANS activity observed after MI. There is consistent evidence, indeed, that depressed patients with coronary heart disease (CHD) or after MI have reduced 24-h HRV and baroreflex cardiac control, which are modulated by PSNS activity on the heart. Based on these findings, nonpharmacological treatments for depression in patients with CHD have been developed. Biofeedback of HRV has recently emerged as an effective bio-behavioral intervention for reducing cardiovascular risk by enhancing PSNS cardiac control in patients with CHD. More importantly, it has been reported that patients with CHD who had received HRV-biofeedback (even after cardiac surgery) showed increased PSNS cardiac control as well as reduced symptoms of depression compared to controls. To date, the time course of depression in relation to physiological modification of indices that reflect both the PSNS and SNS (catecholamines) activities in post-MI patients, and the physiological pathways that mediate the effects of HRV-biofeedback on PSNS cardiac control and depression has not yet been evaluated.

The project will recruit a sample of CHD patients with or without depressive symptoms. The aims of the project can be summarized as follows:

(1) assess HRV and brain electrical activity of the CAN in cardiac patients with or without depression;

(2) examine if theta activity and HRV dysfunctions can be associated in depressive cardiac patients;

(3) assess whether a HRV-Biofeedback intervention can influence the CAN (theta-EEG and HRV) as well as depressive symptoms in the above patients.

Participants CHD patients with and without depressive symptoms will be included. Participants will be recruited through the Unit of Riabilitazione Cardiologica – Ospedale dei Colli – AUSSL 6 Euganea.

The research groups. The PI and the whole research group at UNIPD have developed long-lasting international collaborations in the field of affective, cognitive and behavioral neuroscience, psychiatry, and particularly the area of neuro-visceral integration model for emotion regulation (prof. Juilan Thayer, The Ohio State University), which will provide a solid base for both the proposed projects as well as the planned research methods and trainings.

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EXPERIMENTAL DATA :

To be acquired	X
Already acquired (ready to be used)	

Physiological recording/analysis and procedures will be similar across projects. HRV will be assessed with ECG recording. The ECG will be measured in a modified lead II chest configuration. R-R intervals will be exported to Kubios-HRV Analysis software 2.0 to extract time, frequency and non-linear domains HRV features. The study of non-linear metrics of HRV will be conducted as they have a high informative power in discriminating patients from controls, and in assessing depressive symptoms in medical patients [5]. EEG will be recorded through a pre-cabled high-density 128-channel HydroCel Geodesic Sensor Net and be referenced to the vertex. Time-frequency and source localization analyses will be conducted in Brainstorm. Each system is available at the Department of General Psychology (University of Padua). HRV and EEG features will be used as input for supervised classification algorithms (e.g., neural networks, SVM) to discriminate healthy from depressed subjects. The use of high-density EEG, which exhibits temporal resolution in the millisecond range, together with HRV will provide unique information on the time course and specificity of neural and visceral coupling in healthy individuals as well as in patients with somatic and psychopathological conditions. All patients will undergo (1) an assessment at baseline for biomedical, psychological and psychiatric variables and ECG and EEG recordings (2) a monitoring of the above variables every 3 months for a period of 12 months. In project 1, half of the participants will undergo 5 HRV-biofeedback sessions between the baseline assessment and the first monitoring evaluation. No other specific intervention will be involved in the study, and patients will receive treatment as usual. In project 3 an emotional Go/Nogo task will be included as a measure of attentional inhibition in the processing of unpleasant stimuli.

ETHICS COMMITTEE:

Obtained	*(participants and with depressive subclinical symptoms and controls) **(patients with cardiac diseases)
Conditioned submission	***(patients with depression or Anorexia
Not required	

*Comitato Etico della Ricerca Psicologica Area 17); **Comitato Etico della Ricerca Psicologica Area 17; a further visa to the Ethical Committee of the AUSSL 6 has been submitted; ***a request will be submitted only if a PhD student will be associated to the project