Autonomic Regulation During Acute Mental Stress Is Characterized by Dynamic Interactions

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Abstract

The human organism can be understood as a complex system of dynamic interactions regulating physiological functions to maintain a state of homeostasis. Acute mental stress disrupts homeostasis and triggers a cardiovascular response controlled by the autonomic nervous system. We investigated the effects of acute mental stress on dynamic interactions between 20 vital parameters of haemodynamics, heart rate variability, QT variability, respiration, and skin conductance in 35 healthy subjects. To characterize dynamic interactions, we calculated symbolic transfer entropy between all vital parameters during baseline and acute mental stress. Significant changes were found in the dynamic interactions for 206 of 400 parameter combinations between baseline and acute mental stress ($p < 0.05$, Bonferoni-Holm corrected). Overall, dynamic interactions increased significantly by 9.3 % ($p < 0.001$) compared to baseline. Specifically, acute mental stress caused a 22 % increase of interactions between vital parameters that are dominated by sympathetic and parasympathetic nervous system. Our results indicate that acute mental stress leads to increased autonomic regulation. The characterization of dynamic interactions during acute mental stress provides insights for a better understanding of autonomic regulation processes.

1. Introduction

The human organism seeks a state of homeostasis, where the processes of the organism are in balance. In this state, the organism requires only a small amount of energy to synchronize various processes and organ functions [1]. When the state of homeostasis is disturbed by intrinsic or extrinsic influences, such as stress, the body reacts accordingly, e.g. with the regulation of the cardiovascular system [2]. The purpose of this reaction is to return to homeostasis. Studies showed that the sympathetic nervous system (SNS) takes a dominant role in the autonomic regulation during acute mental stress, while the parasympathetic nervous system (PNS) activity decreases [3, 4]. This behavior can be described as a change in the human state. However, changes in the human state can only be achieved by an interaction between several organ systems [5].

Thus, the aim of this work was to identify and characterize changes in interaction between SNS and PNS in response to an extrinsic influence (acute mental stress) by applying methods from network theory. For this purpose, we chose the symbolic transfer entropy (sTE) as a metric to quantify dynamic interactions, on the basis of various vital parameters extracted from biosignals [5]. Our hypothesis is that acute mental stress leads to increased dynamic interactions between SNS and PNS in order to coordinate autonomic regulation and thus facilitates the process of coping with the stressors.

2. Methods

2.1. Data Material

Participants of the DMDB-MMST performed the Mannheim Multicomponent Stress Test (MMST) to induce acute mental stress [6]. This test combines an algebraic task with affective background images, swelling white noise, negative acoustic feedback, and decreasing response time. 65 healthy participants (age: 25.8 ± 5.1 years) participated in the study. After a baseline measurement of 5 minutes, acute mental stress was induced for 8 minutes during the MMST, shown in Figure 1.

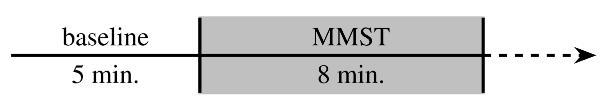

Figure 1. Timeline of the DMDB-MMST study.

During the study, several biosignals were recorded using different acquisition systems [6]. After eliminating incomplete data sets, 35 participants remained for evaluation.

2.2. Signal Processing

To achieve comparability between baseline and MMST, in the middle of each section a window with a length of

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180 s was chosen. For the calculation of heart rate variability (HRV) and QT interval variability (QTV) parameters, the 2DSW algorithm [7] was used to gain precise RR and QT interval series by template-based evaluation of electrocardiograms. The continuous decomposition analysis from the Ledalab toolbox [8] was used to gain tonic activity from skin conductance measurements.

2.3. Vital Parameters

To calculate ultra short-term HRV and QTV parameters from RR and QT interval series, we applied a 90 s sliding window with a step size of 1 s [12]. The skin conductance level SCL is computed from average tonic skin conductance activity. In addition, DMDB-MMST provided haemodynamic and respiratory parameters. Table 1 shows the selection of vital parameters we used. As the multimodal data occurred with different temporal resolution, all vital parameter time series were resampled with 1 Hz for dynamic interaction analysis. The parameters for the dynamic interaction analysis were selected according to their associated classification to SNS and PNS. While parameters derived from HRV and QTV measures have a reported predominance in the literature either by the SNS or PNS [3], this classification cannot be clearly made for haemodynamic or respiratory measures, as these measures are controlled by both nervous systems. Thus, they were summarized by a group called SNS + PNS. The dominant system depends on the human condition and the activity of the respective nervous systems. There is strong evidence that SCL is dominated by the SNS [13].

2.4. Dynamic Interaction Analysis

To study the dynamic interactions between SNS and PNS, the concept of symbolic transfer entropy (sTE) was chosen, which is commonly used to achieve a stable and computationally fast calculation of transfer entropy between two systems [14, 15]. Therefore, we adapted the symbolization introduced by Wessel et al. [16] according to equation (1):

$$S_{x,n} = \begin{cases} 0 : x_{n+1} - x_n < \alpha \cdot s_x, \\ 2 : x_{n+1} - x_n > \alpha \cdot s_x, \\ 1 : otherwise, \end{cases} \tag{1}$$

where $S_{x,n}$ is the symbol of x_n, x_n is the n-th sample of the z-normalized time series of the parameter x, α is the significance threshold for the symbolization, and s_x is the standard deviation of x. For all vital parameters, α was set to 0.05. The symbolization transforms the time series of each parameter into a series of symbols with three different letters: $0, 1, 2$. With a fixed number of three letters, sTE between any combination of parameters was calculated using the JIDT toolbox [17]. For the calculation of sTE, we chose the embedding of the last five seconds based on the Ragwitz criteria, which is already implemented in the auto-embedding function of the JIDT toolbox.

Statistical group comparisons were performed with Wilcoxon signed-rank tests. Bonferoni-Holm correction was applied for multiple tests between groups (e.g. SNS, PNS, SNS + PNS).

Table 1. Vital parameters selected for investigation and their autonomic assignment to sympathetic (SNS) and parasympathetic nervous system (PNS). BSA: Body surface area.

Parameter class	Parameter	Description	Autonomic assignment
Haemodynamic	mBP	Mean blood pressure	SNS + PNS [3]
	CI	Cardiac index (Cardiac output normed to BSA)	SNS + PNS [3]
	EDI	End diastolic index (preload, end-diastolic volume of the left ventricle normed to BSA)	-
	IC	Index of contractillity (maximum blood flow during the left ventricular ejection)	-
	LVET	Left ventricular ejection time	SNS + PNS [3]
	LVWI	Left ventricular work index	SNS + PNS [3]
	SI	Stroke index	SNS + PNS [3]
	TFC	Thoaric fluid content	SNS + PNS [3]
	TPRI	Total peripheral resistance index	SNS + PNS [3]
Heart rate variability	RRmean	Mean duration of RR intervals	SNS + PNS [3]
	pNN50	Proportion of NN intervals greater 50 ms	PNS [9, 10]
	SD1	Standard deviation from the identity line of the Poincare map	PNS [9]
	LF	Absolute power of the low frequency band (0.04 ... 0.15 Hz)	SNS [9]
	HF	Absolute power of the high frequency band (0.15 ... 0.4 Hz)	PNS [9]
QT variability	QTmean	Mean QT interval length	SNS [4]
	STVQT	Short-term QT interval variability	SNS [11]
	LTVQT	Long-term QT interval variability	SNS [11]
Skin conductance	SCL	Skin conductance level (tonic activity)	SNS [11]
Respiration	BR	Breath rate	SNS + PNS [3]
	BRV	Breath rate variability (standard deviation of BR)	SNS + PNS [3]

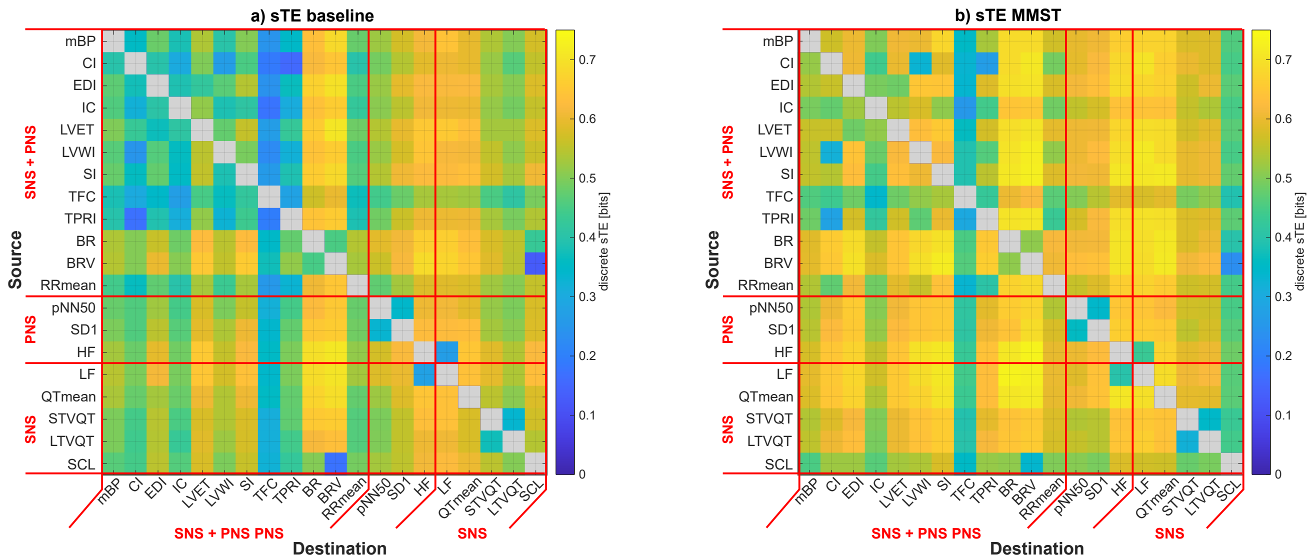

Figure 2. Symbolic transfer entropy (sTE) between any combination of parameters as source and destination, a) during baseline and b) during MMST. Vital parameters, that are not linked to ANS or PNS in the literature are included in the group ANS + PNS. Elements on the main diagonal are colored in gray as sTE is not defined for self-interactions.

3. Results

Figure 2a presents sTE during baseline and Figure 2b presents sTE during MMST. During baseline, dynamic interactions to parameters influenced by both SNS + PNS as destination exhibited a lower mean sTE (-19.9 %) than dynamic interactions to parameters influenced by only one nervous system (SNS or PNS). This was mainly due to parameters of the class haemodynamic measures, see Table 1. Haemodynamic parameters yielded a mean sTE of 0.38 ± 0.1 bits compared with the overall mean of 0.54 ± 0.1 bits at baseline. In contrast, during MMST (Figure 2b), the mean sTE increased significantly by +9.3 % to 0.59 ± 0.09 bits ($p < 0.001$) in all autonomic assignment groups. In vital parameters dominated by SNS + PNS, sTE rose for significant interactions from 0.45 ± 0.13 bits to 0.55 ± 0.11 bits by +22.2 % ($p < 0.001$). Especially haemodynamic measures featured significantly higher mean sTE (+34,2 %, $p < 0.001$) during MMST (0.51 ± 0.1 bits) in comparison to baseline (0.38 ± 0.1 bits). 206 of 400 parameter combinations showed significant differences ($p < 0.05$, Bonferroni-Holm corrected) in dynamic interactions between baseline and MMST as shown in Figure 3. 101 out of 144 (70.1 %) parameter combinations with source and destination being influenced SNS + PNS, showed statistically significant differences in sTE between baseline and MMST. For a better understanding, the total number combinations also include elements from the main diagonal, even if self-interactions are not defined by sTE. In addition, all parameter combinations showed increased sTE during MMST, except for dynamic interactions with SCL as a destination. For SCL, all dynamic interactions with a significant change showed a decrease in sTE (on average -9.6 %), except for dynamic interactions to and from respiration variability.

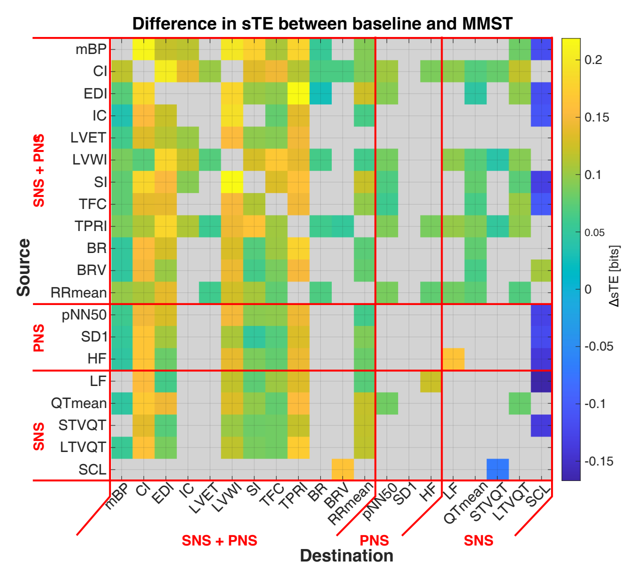

Figure 3. Difference in symbolic transfer entropy between baseline and MMST (ΔsTE). Vital parameter combinations, which did not show a significant difference between baseline and MMST colored in gray.

4. Discussion

Acute mental stress affected dynamic interactions of all investigated vital parameters, both as source and destination, and for most parameters even in both cases. This indicates that acute mental stress alters dynamic interactions between SNS and PNS. Changes in dynamic interactions mainly occur between vital parameters that are influenced by both SNS + PNS. However, there are also changes in dynamic interactions between vital parameters that are dominated by only one autonomic nervous system. For example, all PNS parameters exhibit reduced dynamic interactions (up to -21.7 %) to the SNS dominated parameter SCL when acute mental stress is present. Furthermore, the dynamic interaction from QTmean (SNS) to pNN50 (PNS) increased by +6.8 %. This reflects the physiological expectation of vagal inhibition and sympathetic excitation. For dynamic interactions within parameters that are dominated by both, SNS and PNS, 101 of 144 (76.5 %) interactions show a significant difference between baseline and MMST. This suggests that the dynamic interaction between SNS and PNS is influenced by acute mental stress and a part of the bodily reaction to cope with the stressors. However, during acute mental stress, SNS activity dominates the control over many of the parameters.

The literature describes various pathways of dynamic interactions during acute mental stress, which are studied via neuronal or humoral pathways [18]. Our results coincide with the literature, as we are able to show these dynamic interactions with the information theoretic approach of sTE.

5. Conclusion

In this work, we analyzed the dynamic interactions between parameters controlled by SNS and PNS during acute mental stress and compared it with a baseline measurement. We used the concept of sTE to calculate dynamic interactions between vital parameters representing the activity of the SNS, PNS or both nervous systems. Our results indicate that the interplay between SNS and PNS shows an overall increase in sTE during acute mental stress. At the same time, we observed a decrease in interactions from PNS dominated parameters to SCL, which is dominated by the SNS. In future work, we will analyze the information dynamics during acute mental stress to gain deeper insights on the response to acute mental stress on a participant-individual level. This may help, for example, to develop new strategies for predicting and preventing mental overload in the context of everyday work tasks.

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