# Parasympathetic-Sympathetic causal interaction through the analysis of heart rate variability and electrodermal activity

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***Abstract*— In this preliminary study we presented a novel approach to investigate the interaction between the parasympathetic (PNS) and sympathetic nervous system (SNS) trhough the spectral analysis of the heart rate variability and the electrodermal activity. This new approach was tested to analyze data collected during an isometric handgrip test. Results revealed ...**

## I. Introduction

The autonomic nervous system (ANS) is the primary mechanism to unconsciously regulate most of the bodily functions such as heart rate variability (HRV), respiratory rate, electrodermal activity (EDA), urination, and digestion [1]. The two branches of the ANS, i.e., the parasympathetic (PNS) and the sympathetic nervous systems (SNS), are generally recognized to exert antagonistic effects on the regulation of autonomic functions. However, this opposing interplay is not algebraically additive, but complicated interactions exist [2]. Indeed, plenty of experimental and clinical studies have demonstrated the presence of multiple interactions between PNS and SNS that are mediated through several pathways and mechanisms at both central and peripheral levels [3].

In this preliminary study, we aim at characterizing the directional interdependence between the PNS and SNS through the analysis of two widely used ANS correlates such as the HRV and the EDA. In fact, on the one hand, the estimation of the high frequency (HF) components of the HRV spectrum is commonly considered a reliable measure of the PNS activity on cardiac functioning [4]. On the other hand, the spectral power of the EDA in the range of 0.045 to 0.25 Hz (EDASYMP) has been recently presented as an index of the SNS activity under cognitive, orthostatic and physical stress (handgrip) conditions [5]. To detect and quantify the bilateral causal interactions between the two branches of the ANS, we adopted a multivariate autoregressive (MVAR) model [6]. Due to the time-variant relationships between these signals, we applied a modified recursive Kalman filter to track changes in the model parameter.

## II. Materials and Methods

Twenty-five healthy subjects (aged XX $\pm$ XX years) underwent an isometric handgrip test. The protocol consisted of 3 min of resting-state (rest0) and 2 min during which the subject was asked to tighten a small hard ball in his/her dominant hand at the maximum contraction strength (hg). The ECG and EDA signals were recorded using the BIOPAC MP 150 system with a sampling frequency of 500 Hz.

EDA signal represents changes in the skin conductance of the non-dominant hand and it is a manifestation of the activity in sweat glands. Since sweat glands are innervated by the SNS, EDA is considered an ideal way to estimate the SNS activity. ECG signals were used to detect R-peaks in order to generate RR time series that were subsequently resampled at 4 Hz (HRV). The EDA signals were also resampled at 4 Hz.

From HRV and EDA, we estimated the HF power spectrum and EDASYMP, respectively. More in details, the time-frequency representation of both the HRV and EDA signals were calculated using the smoothed pseudo-Wigner-Ville distribution method (SPWVD) [7], as it is shown in eq. 1:

$$\eta_x(f,t) = \int_{-\infty}^{\infty} \phi_d(\tau) \left[ \int_{-\infty}^{\infty} \phi_t(t-\nu) x(\nu - \frac{\tau}{2}) \right. \\ \left. x^*(\nu - \frac{\tau}{2}) d\nu \right] e^{-j2\pi f \tau} d\tau, \tag{1}$$

where: $\phi_d$ and $\phi_t$ are smoothing functions (the first an exponential window and the latter a rectangular window), and $x(t)$ represents the HRV and EDA time series. We applied SPWVD because it provides better time-frequency resolution with respect to non-parametric linear methods [8].

## III. Parasympathetic-sympathetic causal interaction (PSCI)

For each subject, the HF and EDASYMP time-series were used to construct bivariate autoregressive models from which the HF-EDASYMP causal interactions were estimated. In particular, we exploited the framework presented in [6] to estimate time-varying (TV-) model coefficients based on an optimized kalman-filter approach. Furthermore, the heteroskedasticity of model residuals was evaluated in order to take into account possible TV- model residual variances. Indeed, this represents a major issue in the estimation of coupling measures obtained from TV-MVAR models, leading to inaccuracies in both strength and directionality of coupling estimates. To properly compare the amount of interaction across different subjects we estimated the generalized Partial

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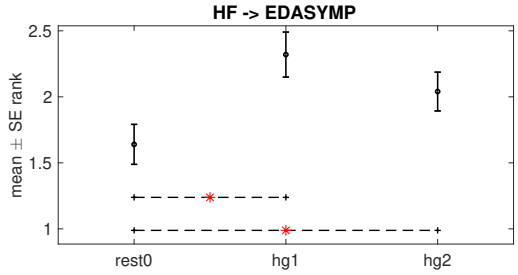


Fig. 1. Within-subject ranks of the HF→EDASYMP index obtained for the three sessions. Statistical pairwise comparisons found significant differences in the cases indicated by the asterisks.

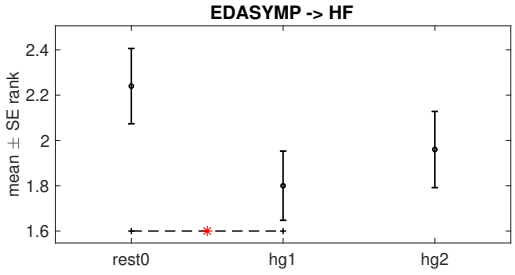


Fig. 2. Within-subject ranks of the EDASYMP→HF index obtained for the three sessions. Statistical pairwise comparisons found significant differences in the cases indicated by the asterisks.

Directed Coherence (gPDC) [baccala2007,sato2009] starting from the time-varying model coefficients and covariances. This estimator results in a scale-invariant estimator of granger-causal interactions between different time-series. The statistical significance of observed gPDC was assessed through a phase-randomization approach [thieler 1992]. Group level analysis was performed by averaging surrogates distributions from each subject. The averaging was performed for each direction of interaction, each frequency, and each time-window, i.e for each $(i, j, \omega, t)$. Statistically significant causality was obtained by comparing average gPDC across subjects with the group-level null-distribution. Multiple testing was controlled with standard false discovery rate procedure ($\alpha_{FDR} = 0.05$). Finally, differences between gPDC in REST and HG conditions were analyzed.

### A. Statistical analysis

An intersubject Wilcoxon test compared the PSCI indexes among the resting session and the first and second half of the handgrip session. The analysis was performed for both HF→EDASYMP and EDASYMP→HF directions. False discovery rate was controlled through the Benjamini-Hockberg-Yekuteli correction for multiple testing.

## IV. Results

The causality analysis evidenced significant different interactions based on the experimental condition (Fig. 1 and 1). Specifically, we observed a significant increase in the flow of information going from HF to EDASYMP during the HG task with respect to the REST condition (Fig. 1). On the other hand a decrease of the EDASYMP to HF interaction was observed during HG (Fig. 2).

## V. Discussion and Conclusion

In this preliminary study, we propose a novel approach to investigate the directional interaction between the PNS and SNS during a handgrip task. The activity of the PNS (HF) and SNS (EDASYMP) were estimated through the spectral analysis of the HRV and the EDA respectively, by using the SPWD method for a better time resolution. A TV-MVAR approach quantified the causal interaction between HF and EDASYMP revealing a significant increase in the information sent from the PNS to the SNS during the whole handgrip phases. Contrarily, the information sent from the SNS to the PNS significantly decreased at the beginning of the handgrip task and then goes back at the resting level.

## References

[1] L. K. McCorry, "Physiology of the autonomic nervous system," *American journal of pharmaceutical education*, vol. 71, no. 4, p. 78, 2007.

[2] M. N. Levy, "Brief reviews: sympathetic-parasympathetic interactions in the heart," *Circulation research*, vol. 29, no. 5, pp. 437–445, 1971.

[3] K. Ondicova and B. Mravec, "Multilevel interactions between the sympathetic and parasympathetic nervous systems: a minireview," *Endocr Regul*, vol. 44, no. 2, pp. 69–75, 2010.

[4] M. V. Kamath and E. L. Fallen, "Power spectral analysis of heart rate variability: a noninvasive signature of cardiac autonomic function." *Critical reviews in biomedical engineering*, vol. 21, no. 3, pp. 245–311, 1993.

[5] H. F. Posada-Quintero, J. P. Florian, A. D. Orjuela-Cañón, T. Aljama-Corrales, S. Charleston-Villalobos, and K. H. Chon, "Power spectral density analysis of electrodermal activity for sympathetic function assessment," *Annals of biomedical engineering*, vol. 44, no. 10, pp. 3124–3135, 2016.

[6] K. Kostoglou, A. D. Robertson, B. MacIntosh, and G. D. Mitsis, "A novel framework for estimating time-varying multivariate autoregressive models and application to cardiovascular responses to acute exercise," *IEEE Transactions on Biomedical Engineering*, 2019.

[7] M. Orini, R. Bailón, L. T. Mainardi, P. Laguna, and P. Flandrin, "Characterization of dynamic interactions between cardiovascular signals by time-frequency coherence," *IEEE Trans. on Biom. Eng.*, vol. 59, no. 3, pp. 663–673, 2012.

[8] S. Pola, A. Macerata, M. Emdin, and C. Marchesi, "Estimation of the power spectral density in nonstationary cardiovascular time series: assessing the role of the time-frequency representations (tfr)," *IEEE Transactions on Biomedical Engineering*, vol. 43, no. 1, p. 46, 1996.