The Role of EEG Electrical Reference in the Assessment of Functional Brain-Heart Interplay: A Preliminary Study

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Abstract— **Recent studies have proposed computational models for a functional brain-heart interplay (BHI) assessment based on electroencephalography (EEG). Nevertheless, the role of the EEG electrical reference on such BHI estimates has not been investigated yet. Here we present a pilot study assessing BHI in 4 minutes resting-state in 10 healthy subjects through methods including heartbeat-evoked potentials (HEP) and oscillations, Maximal Information Coefficient, and our recently proposed model based on Synthetic Data Generation (SDG). EEG signals were re-referenced to the Cz channel, common average, mastoids, and Laplacian. Results for EEG power in the α band indicate that the most significant differences between BHI methods are with the Laplacian reference while a higher agreement exists between HEP and SDG approaches.**

I. INTRODUCTION

Functional brain-heart interplay (BHI) continuously affects bodily and central functions [1]. The importance of a proper BHI assessment is directly linked to emerging evidence on the active role of the heart to cognition and associated disorders [1]–[4]. From a methodological viewpoint, BHI estimates may be gathered using simultaneous Electroencephalogram (EEG) and Heart Rate Variability (HRV) recordings to compute heartbeat-evoked potentials (HEP) [5]. Further BHI assessments include heartbeat-evoked oscillations (HEO) [7], functional linear or nonlinear correlation measurements between time-varying EEG and HRV components, such as Maximal Information Coefficient (MIC) [8], and the coupling estimation from computational models for EEG and HRV Synthetic Data Generation (SDG) that are mathematically combined to estimate the directional strength [9]. In this frame, HRV-derived powers within the high and low frequency bands may be used for the estimation of vagal and sympathovagal activities, respectively [6].

While EEG electrical reference may strongly affect EEG-based markers [10], its impact on functional BHI assessment has not been investigated yet. To this end, in this preliminary study we investigate group-wise BHI changes from SDG, HEP, HEO, and MIC methods across four commonly used EEG-referencing options including the Cz electrode, common average, mastoids average, and Laplacian method [11].

II. MATERIALS AND METHODS

A. Data acquisition and processing

High-density 128 channels EEG (Electrical Geodesics, Inc) and one-lead ECG were gathered from 10 healthy young adults during a 4-minute resting state. Data were sampled at 500 Hz and referenced to the Cz channel.

All signals were bandpass filtered between 0.5-45 Hz. On the EEG series, a wavelet-enhanced independent component analysis was performed to remove large movements and cardiac field artefacts. Channels located on the face and neck were not considered for further analysis. EEG channels were considered corrupted if the area under the curve exceeded 3 standard deviations of all channels mean, or if the weighted-by-distance correlation with their neighbors was below $R_2 = 0.6$. Corrupted channels were replaced using a weighted-by-distance interpolation of neighbors. EEG data is then re-referenced using 4 methods: Cz electrode, Common Average, Mastoids Average or Laplacian Method [11]. A subset of 64 channels were selected for this study according to the 10-10 system. EEG α-band series (8-12 Hz) are computed using FFT algorithm within 2s time windows with 50% overlap and 0.5 Hz step. Electrocardiogram processing includes automatic R-peak detection using a template correlation approach with a subsequent visual inspection and eventual correction to derive HRV series. Series of high-frequency power (HRV-HF within 0.15-0.4 Hz) are computed from HRV series using an adapted Wigner-Ville distribution [12].

B. Brain-Heart Interplay Assessment

Functional BHI was quantified through the following approaches:

1) *Synthetic Data Generation* (SDG) model assesses bi-directional interplay between EEG oscillations and HRV [9]. Here the interplay is computed from HRV-HF to EEG α-band and its time-varying dynamics was averaged for further analysis.

2) *Heartbeat-evoked potential* (HEP) is the neural response triggered by each heartbeat [5]. For each subject, HEP is computed by averaging EEG epochs within the 200-400ms interval with respect to R-peaks. Time-varying dynamics is condensed by averaging for further analysis.

3) *Heartbeat-evoked oscillations* (HEO) similarly to HEP, EEG oscillations were locked to the R-peak as proposed in [7]. The evoked oscillations were studied in the α-band. EEG epochs were locked to the R-peak between 200-400 ms, with relative change baseline respect -300 to -200 ms interval. Time-varying dynamics is averaged for further analysis.

4) *Maximal information coefficient* (MIC) aims to find linear/non-linear functional associations between EEG power

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and HRV series [4], [8]. In this study, the coefficient is computed between the EEG α-band and HRV-HF time series.

C. Group-wise statistics and correlation analysis

Group-wise statistics included Spearman's correlation coefficients computed between each pair of referencing methods and for each BHI estimation method per channel. P-values are computed from the t-distribution approximation. Results are then summarized as the percentage of EEG channels (ch) with significant p-value ($p<0.05$), and correlation coefficients (r) median ± median absolute deviation (MAD) calculated across all EEG electrodes. Correlations were considered significant if ch>50% and median $r \geq 0.6$.

III. RESULTS

Z-scored, group-wise topographic maps for all referencing options and BHI estimates are shown in Fig 1, whereas results from the non-parametric correlation analysis are shown in Table I.

To a qualitative extent, group-wise topographies between BHI estimates show high similarities between SDG and HEP methods for all references (see Fig 1). Moreover, while MIC seems to be associated with heterogeneity between reference methods, Laplacian reference shows the most significant differences between references and estimation methods. Quantitatively, common average and mastoids, as well as common average and Cz references show similarities between different BHI methods (see Tab. I).

TABLE I.   RE-REFERENCE WIITHIN BHI ESTIMATES CORRELATIONS

	SDG	HEP	HEO	MIC
Cz-Average	**ch = 91%** **r = 0.8± 0.1**	ch = 44% r = 0.6± 0.3	**ch = 63%** **r = 0.7± 0.2**	ch = 9% r = 0.2± 0.3
Cz-Mastoids	ch = 47% r = 0.6± 0.2	ch = 6% r = 0.2± 0.3	**ch = 52%** **r = 0.6± 0.2**	ch = 6% r = 0.2± 0.3
Cz-Laplacian	ch = 38% r = 0.6± 0.2	ch = 22% r = 0.4± 0.2	ch = 19% r = 0.3± 0.3	ch = 2% r = 0.1± 0.2
Average-Mastoids	**ch = 89%** **r = 0.8± 0.1**	**ch = 53%** **r = 0.7± 0.1**	**ch = 70%** **r = 0.7± 0.2**	ch = 16% r = 0.3± 0.2
Average-Laplacian	ch = 39% r = 0.6± 0.2	ch = 33% r = 0.6± 0.2	ch = 19% r = 0.3± 0.3	ch = 5% r = 0.1± 0.3
Mastoids-Laplacian	ch = 30% r = 0.5± 0.2	ch = 16% r = 0.3± 0.2	ch = 20% r = 0.3± 0.3	ch = 5% r = 0.1± 0.3

Bold indicates significant outputs (ch>50% and $r \geq 0.6$)

IV. DISCUSSION

In this preliminary study we reported on the role of EEG electrical reference for a functional BHI assessment. Our findings suggest that EEG electrical reference significantly influences the quantification of functional BHI. Particularly, while the Laplacian reference strongly biases the BHI estimation, the Cz, common average, and mastoids average references show consistency for BHI estimates from SDG and HEP. While the MIC shows low correlations between reference methods, HEO shows good correlations but different topography between references.

Indeed, further data is needed to investigate the role of EEG reference over different experimental tasks, different EEG frequency bands, and with a larger set of subjects. Different methods for BHI estimation are likely to measure

different functional activities of the underlying physiological processes. Although preliminary, these findings highlight the important role of EEG referencing choice for BHI estimation.
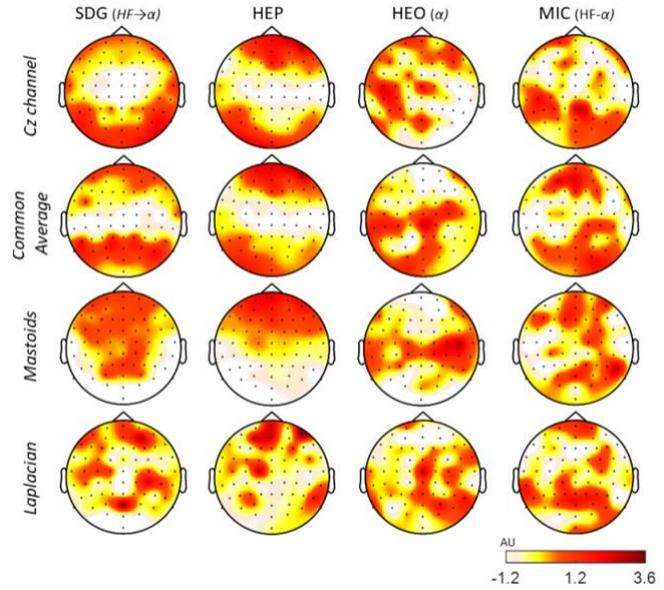

Fig 1. Brain-Heart Interplay estimates (group median and z-scored, for visualization purposes only). AU: Arbitrary Units

REFERENCES

[1]   D. Azzalini *et al*, "Visceral Signals Shape Brain Dynamics and Cognition," *Trends in Cognitive Sciences*, vol. 23, no. 6, pp. 488–509, Jun. 2019.

[2]   J. Terhaar *et al*, "Heartbeat evoked potentials mirror altered body perception in depressed patients," *Clin Neurophysiol*, vol. 123, no. 10, pp. 1950–1957, Oct. 2012.

[3]   G. Valenza *et al*, "Uncovering brain–heart information through advanced signal and image processing," *Philosophical Transactions of the Royal Society A*, vol. 374, no. 2067, p. 20160020, May 2016.

[4]   G. Valenza *et al.*, "Combining electroencephalographic activity and instantaneous heart rate for assessing brain–heart dynamics during visual emotional elicitation in healthy subjects," *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, vol. 374, no. 2067, p. 20150176, May 2016.

[5]   R. Schandry *et al.*, "From the heart to the brain: a study of heartbeat contingent scalp potentials," *Int. J. Neurosci.*, vol. 30, no. 4, pp. 261–275, Nov. 1986.

[6]   Acharya, U.R. *et al.* Heart rate variability: a review. Medical and biological engineering and computing, 44(12), pp.1031-1051, 2006

[7]   F. Grosselin *et al*, "CARE-rCortex: A Matlab toolbox for the analysis of CArdio-REspiratory-related activity in the Cortex," *J. of Neuroscience Methods*, vol. 308, pp. 309–316, Oct. 2018.

[8]   D. N. Reshef *et al.*, "Detecting Novel Associations in Large Datasets," *Science*, vol. 334, no. 6062, pp. 1518–1524, Dec. 2011.

[9]   V. Catrambone *et al*, "Time-Resolved Directional Brain-Heart Interplay Measurement Through Synthetic Data Generation Models," *Ann Biomed Eng*, vol. 47, no. 6, pp. 1479–1489, 2019.

[10]   D. Hagemann *et al*, "The quest for the EEG reference revisited: a glance from brain asymmetry research," *Psychophysiology*, vol. 38, no. 5, pp. 847–857, Sep. 2001.

[11]   P. L. Nunez *et al*, "A theoretical and experimental study of high resolution EEG based on surface Laplacians and cortical imaging," *Electroencephalography and Clinical Neurophysiology*, vol. 90, no. 1, pp. 40–57, Jan. 1994.

[12]   M. Orini et al, "Characterization of dynamic interactions between cardiovascular signals by time-frequency coherence," *IEEE Trans Biomed Eng*, vol. 59, no. 3, pp. 663–673, 2012.