

## Effectiveness of an R-based software to detect closed-loop cardiovascular interactions and baroreflex impairment in human subjects from the EUROBAVAR data set

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We recently developed an R-based software that could model closed loop cardiovascular interactions. In this study, we applied this tool on the EUROBAVAR data set to further test its applicability. This set consists of 21 human beat-to-beat blood pressure recordings with their corresponding inter-beat intervals (IBI) obtained during supine rest and standing positions. Of these subjects, two are known to have a baroreflex impairment. The aim of this work is to test the effectiveness of our software to identify cardiovascular regulatory mechanisms and baroreflex impairment from these data. After downloading the recordings, we first uploaded each recording into our software to model the interactions present between systolic blood pressure (SBP) and IBI by employing a wavelet detrending and multivariate autoregressive modeling algorithm. Then, our software estimated causal coherence and Gaussian-weighted baroreflex sensitivity (BRS) indexes from each model at the low frequency (LF, 0.04-0.15 Hz, sympathetic) and high frequency (HF, 0.15-0.4 Hz, parasympathetic) bands. Immediate variability transfer from SBP to IBI was also computed for each subject. Estimates were compared using the Wilcoxon test for paired samples. Our results showed that, when standing, the estimates of only two subjects, B005 and B010, were below percentile P10 of the BRS distribution (0.719 ms/mmHg at HF, 1.678 ms/mmHg at LF) at both bands. A literature review indicated that these two subjects had a baroreflex impairment. In non-baroreflex-impaired subjects, causal coherence from IBI to SBP at LF was significantly predominant at rest when compared with the coupling from SBP to IBI ( $p < 0.001$ ). This predominance disappeared during standing due to changes in the couplings, suggesting a baroreflex interaction. Closed-loop BRS supine-to-standing ratios in these subjects were  $1.69 \pm 0.93$  (LF band) and  $3.1 \pm 1.32$  (HF band), showing a significantly decreased BRS during standing position ( $p < 0.01$ , LF;  $p < 0.001$ , HF). Immediate transfer also decreased during standing ( $p < 0.001$ ). In conclusion, our software managed to evaluate causal closed-loop interactions between cardiovascular variables from the data set, evidencing a baroreflex coupling, and was able to identify baroreflex impairment. Thus, this allows it to be a useful tool for baroreceptor evaluations.

Keywords: cardiovascular regulation, baroreflex impairment, spectral analysis, autoregressive models.

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