Detection of ST-Segment Variation in ECG Using Transfer Entropy

Ilya Potapov, Esa Räsänen

Laboratory of Physics, Tampere University of Technology, Finland

Abstract

Many severe heart dysfunctions cause changes in the ST-segment of ECG. We hypothesize that the change in ST affects the degree of coupling between the QT time intervals and the heart rate (HR, inverse of the inter-beat interval RR). Therefore, we analyze the informational transfer between the coupled dynamics of QT and RR to detect the ST segment variation. We use the transfer entropy method allowing for a quantitative and uni-directional measure of coupling between two temporal processes. We analyze the data from ST variation patients and normal individuals. We show that the RR-to-QT information transfer for the ST group is larger than the corresponding transfer for the normal group. This indicates a larger degree of uncertainty in QT dependence on RR. Moreover, on average the segments of ST-episodes have the associated RR-to-QT transfer larger than the non-ST episodes. Finally, we demonstrate that the ratio between intra- and inter-subject diversity of the QT-RR relationship can have a characteristic value for the segments of ST episodes. We conclude that the degree of inter-dependence between QT and RR can be a marker of the ST variation pathology.

1. Introduction

Severe heart dysfunctions, like myocardial ischaemia or infarction, are associated with abnormalities in the ST-segment, a flat isoelectric section of ECG. Such malfunctions of the heart cause ST-segment depression or elevation. Reliable detection of such abnormalities can lead to the early preventive therapies of the associated diseases [1].

In this work, we hypothesize that not only the isoelectrical properties of the ST-segments are disturbed during pathological manifestations, but also the duration of the ST segment, and hence the QT segment, changes. Thus, the dynamical coupling between QT and RR intervals should be disturbed as well.

In order to verify our conjectures we measure the degree of dynamical coupling between the QT time interval and the inter-beat interval (RR) by the transfer entropy method [2]. We compare the results with previous studies [3] of the transfer entropy on the normal symptomless subjects. Additionally, we compare normal subjects and specifically the abnormal and normal ST-segment episodes of the patients with ST-segments pathologies. We draw the distinction between these groups by comparing the information flows between QT and RR.

2. Methods

Transfer entropy (TE) estimates information transfer (defined in Shannon terms) from the *source* process to the *destination* process. This is achieved by calculating the amount of information that the source preceding samples provide about the next sample of the destination in the context of the destination preceding samples [2].

The relation between the preceding samples and the next sample of, e.g., QT series in the RR→QT transfer estimation is formally written as [2]:

$$\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}} = \sum_{\mathrm{i}} \mathrm{p}(\mathrm{QT}_{\mathrm{i}}, \mathrm{QT}^{(\mathrm{k})}_{\mathrm{i}-1}, \mathrm{RR}^{(\mathrm{n})}_{\mathrm{i}-1}) \times \\ \times \log_2 \frac{p(\mathrm{QT}_{\mathrm{i}}|\mathrm{QT}^{(\mathrm{k})}_{\mathrm{i}-1}, \mathrm{RR}^{(\mathrm{n})}_{\mathrm{i}-1})}{p(\mathrm{QT}_{\mathrm{i}}|\mathrm{QT}^{(\mathrm{k})}_{\mathrm{i}-1})},$$

where $p(x)$ is a probability distribution, $p(x|y)$ is a conditional probability, $\mathrm{QT}^{(\mathrm{k})}_{\mathrm{i}-1}$ and $\mathrm{RR}^{(\mathrm{n})}_{\mathrm{i}-1}$ are k and n preceding samples (from $i-1$ backwards) of QT and RR series, respectively. The sum is taken over all states i of the process. The resulting TE measure is in bits of information and is the average over the process realizations. In this study we vary RR history (n), whereas QT history (k) remains equal to one heartbeat, i.e. $k = 1$.

We use Java Information Dynamics Toolkit (JIDT version 1.3.1) for TE calculations [4] with Kraskov-Stögbauer-Grassberger (KSG) probability estimation [5] (algorithm no. 1), 4 nearest neighbors, and default values for other parameters.

2.1. Data

We downloaded the raw ECG signals from PhysioNet [6] ("MIT-BIH Normal Sinus Rhythm" and "MIT-BIH Long Term" databases for the normal cases, $N = 25$,

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and "Long-Term ST" database for the patients with ST segment pathologies, $N = 86$). Then, we extracted RR and QT intervals using the provided software [6–8] and discarded low quality signals. The extracted RR and QT values were guaranteed to be from the contiguous ECG regions of at least 500 heartbeats long. In this work we pursue two lines of research: i) on the contiguous regions *merged* into a single time series per subject and ii) on each of the contiguous regions. Moreover, given a very detailed annotation of the ST database [9] we are able to further divide the contiguous regions into the ST variation episodes and the episodes without ST variation (non-ST) within a single ECG signal.

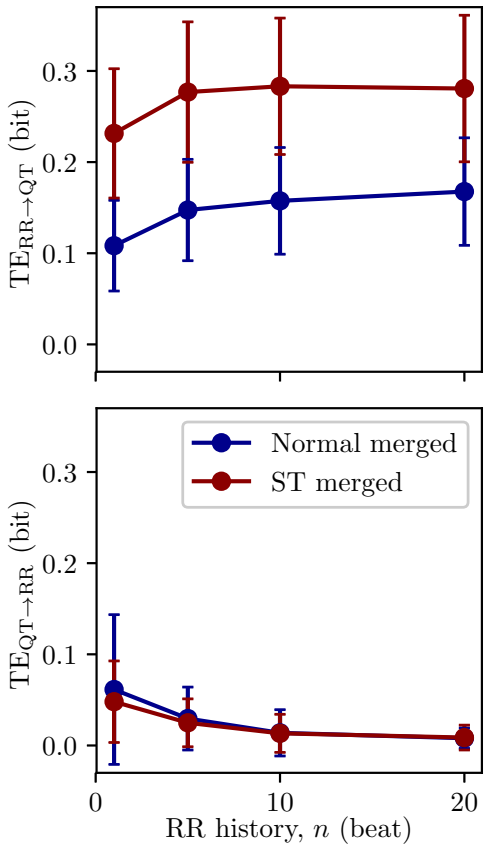

Figure 1. $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ is larger for the patients with ST abnormalities than for the normal subjects in case of the merged time series. $\mathrm{TE}_{\mathrm{QT}\to\mathrm{RR}}$ undergoes no significant change for the patients with ST abnormalities. Format: mean $\pm$ standard deviation.

3. Results

3.1. Information flows

It was shown in Ref. [3] that for healthy individuals RR $\to$ QT information flow is larger than the opposite QT $\to$ RR and that the asymmetry increases with the increased RR history n.

We confirm that the asymmetry holds for the ST-variation patients as well (Fig. 1), however the actual information flow measured by $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ for the ST patients is significantly larger than for normal subjects at all considered n. This indicates that the QT dependence on RR is larger for the patients with the ST pathologies than for the healthy individuals. In other words, QT follows more closely RR in the ST case than in normal conditions.

Note that in this work by "influence" or "dependence" we do not mean causality, but rather correlation between the coupled processes.

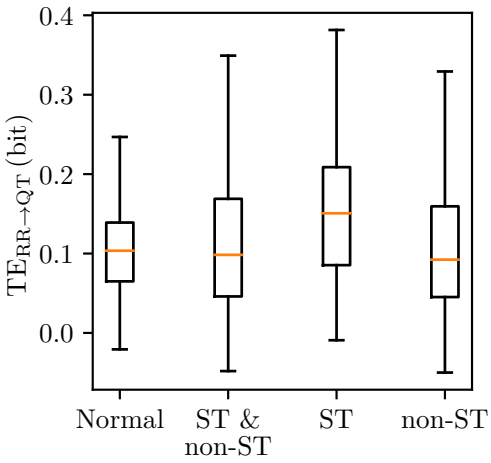

Figure 2. $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ shows no difference between the ST-variation (ST & non-ST) and Normal subjects when separate contiguous segments are analyzed (cf. Fig. 1). However, $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ is larger for ST episodes specifically than for both Normal subjects and non-ST episodes of the ST-variation patients. The orange lines show the median of the distributions. The upper and lower boundaries of the box depict the 1st and the 3rd quartiles of the distributions. The lines extend further to cover additional 1.5 of the interquartile range (length of the box). $n = 10$, $k = 1$.

The study of the history, or preceding samples, may have an apparent limitation in case of the merged signals. Namely, for some samples close to the merged points the history includes samples from two distinct contiguous regions, which are separated by a longer than one heartbeat time span in the original ECG signal.

Hence we study the contiguous regions of ECG separately. For convenience we consider only $n = 10$ heartbeats and $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$. First, we analyze all contiguous regions of ECG (without distinguishing between ST and non-ST episodes) in the two datasets ("Normal" and "ST & non-ST" in Fig. 2) and find no difference in $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ between the two groups of subjects ($P = 0.07$ unpaired t-test).

Using this approach we do not specifically distinguish between the actual ST-variation episodes and episodes without ST variation. However, the detailed annotation [9] of the ST database allows for such distinction. Next, we consider the contiguous ECG regions of the ST-variation episodes (ST) and those without such episodes (non-ST) and compare the two with the healthy subjects' contiguous regions (Normal, Fig. 2). The ST distribution for $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ is significantly larger than the healthy subject distribution ($P < 10^{-14}$, unpaired t-test) and the non-ST distribution ($P < 10^{-20}$, unpaired t-test).

3.2. Intra- and inter-subject diversity

Some authors hold (e.g. in Ref. [10]) that the QT-RR relationship is characterized by intra-subject stability and inter-subject variability. Thus, for example, it is not plausible to describe the relationship using universal equalities. Using our approach one can quantify the individual QT-RR relationship using $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ and $\mathrm{TE}_{\mathrm{QT}\to\mathrm{RR}}$. Note that in this approach the measured interval values of QT and RR dictate the level of the resulting information transfers.

Following Ref. [10] we quantify the intra-subject diversity by the *average standard deviation of the TE distributions for contiguous regions from individual ECG recordings*, while the inter-subject diversity is *the standard deviation of the means of the corresponding TE distributions*. In this study we kept minimum number of contiguous regions per subject equal to 3. This way, we have maximized the number of subjects and improved the estimation of the inter-subject diversity (which was especially sensitive in the case of $\mathrm{TE}_{\mathrm{QT}\to\mathrm{RR}}$). The minimum number of regions, on the other hand, was shown not to affect much the intra-subject diversity for the two transfers.

Table 1. Intra- and inter-subject diversities for $\mathrm{TE}_{\mathrm{QT}\to\mathrm{RR}}$. N is the number of subjects that have at least 3 contiguous regions.

Group (N)	Intra (bit)	Inter (bit)	Intra/Inter
Normal (22)	0.010	0.020	0.491
ST (41)	0.012	0.019	0.618
Non-ST (83)	0.012	0.014	0.832

Our results suggest that the intra-subject stability is observed only in the case of $\mathrm{TE}_{\mathrm{QT}\to\mathrm{RR}}$ (Table 1), i.e., intra-subject diversity is significantly less than inter-subject diversity, whereas $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ demonstrates significantly larger intra-diversity than inter-diversity. Notably, the ST episodes show nearly similar intra- and inter-subject diversities for the RR→QT transfer as opposed to normal and non-ST episodes (Table 2).

Table 2. Intra- and inter-subject diversities for $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$. N is the number of subjects that have at least 3 contiguous regions.

Group (N)	Intra (bit)	Inter (bit)	Intra/Inter
Normal (22)	0.048	0.039	1.223
ST (41)	0.058	0.057	1.005
Non-ST (83)	0.063	0.047	1.347

To further demonstrate these inequalities we visualize the individual TE distributions (intra-diversity) and the corresponding distributions of means (inter-diversity) in Fig. 3. One can see from the figure that the mean $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ distribution for the ST episodes is significantly wider than the corresponding distribution for normal subjects. Nevertheless, the standard deviation of the ST distribution is comparable to those of the individual distributions, however, in the case of the normal subject distribution its standard deviation is significantly less on average than those of the individual distributions. Thus, the inter-subject diversity does not undergo significant variability in $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ values.

4. Discussion

We used the recently proposed methodology for characterization of the mutual dynamics of QT and RR intervals [3] to compare healthy subjects with patients with the ST-variation pathologies.

We showed that the RR→QT transfer is larger than the QT→RR transfer for the ST-variation subjects. Additionally, no significant differences in information transfers were found between the normal and ST groups, when analyzing contiguous regions of ECG recordings. However, when analyzing particularly the ST- and non-ST episodes of the ST group, the ST-episodes reveal significantly higher $\mathrm{TE}_{\mathrm{RR}\to\mathrm{QT}}$ values than the non-ST episodes and contiguous regions of healthy subjects.

Finally, we found intra-subject stability and inter-subject variability only in the case of the QT→RR transfer. However, for the RR→QT transfer we found that the intra-subject diversity is larger than the inter-subject diversity for the healthy and non-ST regions, meaning that the variability between subjects is less than the variability within subjects. Noteworthy, the ST-episodes show almost similar intra- and inter-subject diversities for the RR→QT transfer, which can be further used in detection of the ST-

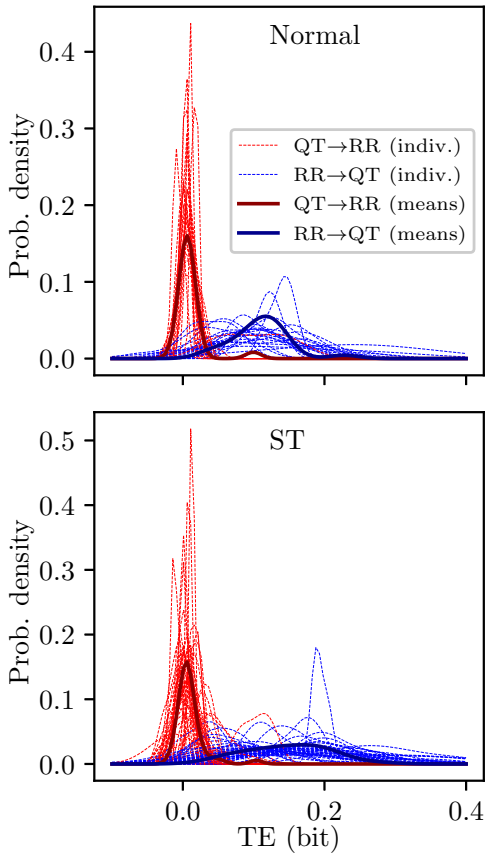

Figure 3. TE distributions for all contiguous regions of each individual (indiv.) and distribution of means of individual distributions. $n = 10$, $k = 1$.

variation episodes.

5. Conclusions

We conclude that the characteristic features of the information flows (notably those of the RR→QT flow) can be used in detection of the ST-segment variation and in classification between ST- and non-ST-episodes of patients with ST-segment pathologies.

Acknowledgements

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Address for correspondence:

Name: Ilya Potapov, PhD
Full postal address: Laboratory of Physics, Tampere University of Technology, P.O. 553, 33101 Tampere, Finland
E-mail address: ilya.potapov@tut.fi