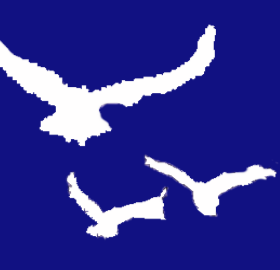


ESTIMATED PREEJECTION PERIOD (PEP) BASED ON THE DETECTION OF THE R-WAVE AND DZ/DT-MIN PEAKS IN ECG AND ICG

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Introduction

Hyperactivity of the sympathetic nervous system (SNS) may be paramount to the detrimental effects of stress on cardiovascular health. The Pre-Ejection Period (PEP) is widely used to measure SNS activity during subjects' daily routine. PEP measurement heavily relies on the accurate detection of ECG and ICG landmarks that are difficult to detect due to lapses in beat-to-beat signal quality for instance introduced by movement. Large scale epidemiological studies would benefit from a measure that relies on landmarks in ECG and ICG that are less sensitive to noise and do not show rater dependency.

Detection of the Q-wave onset and B point (PEP) is sometimes visually challenging. In this study the PEP was divided into the QR and RB interval to answer the following :

Can the QR interval be approximated by a fixed interval as is common practice in most studies using PEP?

Can the seemingly strong relationship between the dZ/dt-min peak (C-point) and B point be utilized to estimate the B point location?

Does PEP from a fixed QR interval plus a B point obtained by regression from dZ/dt-min peaks adequately predict the actual PEP across subjects and a wide range of conditions?

It was tested whether the formula for the estimated PEP obtained from data in a laboratory study can be applied to a confirmatory ambulatory study.

Materials and Methods

Laboratory Study

Experimental Condition	Duration (min)
Resting baseline	4
Paced breathing (BF 32)	1
Paced breathing (BF 20)	1
Paced breathing (BF 12)	1
Paced breathing (BF 6)	2
Paced talking (Words)	2
Paced talking (Numbers)	4
Stroop color word conflict	4
Serial subtraction	4
Posture: Sitting	4
Posture: Supine	4
Posture: Standing	4
Humoristic movie	4
Cold Pressor	3
Handgrip	4
Bicycle ergometer (Baseline)	4
Bicycle ergometer (Low) (60rpm)	4
Bicycle ergometer (100W) (60rpm)	4
Bicycle ergometer (Recovery)	4

Ambulatory Study

Experimental Condition	Duration (min)
Baseline sitting	4
Posture: standing 1	3
Posture: supine 1	3
Posture: sitting 1	3
Posture: standing 2	3
Posture: sitting 2	3
Tone avoidance	2
Walking outside	2
Walking & talking	3
Staircase climbing	3
Bicycle ergometer (50W) (60rpm)	4
Bicycle ergometer (100W) (60rpm)	4
Bicycle ergometer (150W) (60rpm)	4
Bicycle ergometer (Recovery)	4
Treadmill walking (5 km/h)	4
Treadmill walking (6 km/h)	4
Treadmill walking (8 km/h)	4

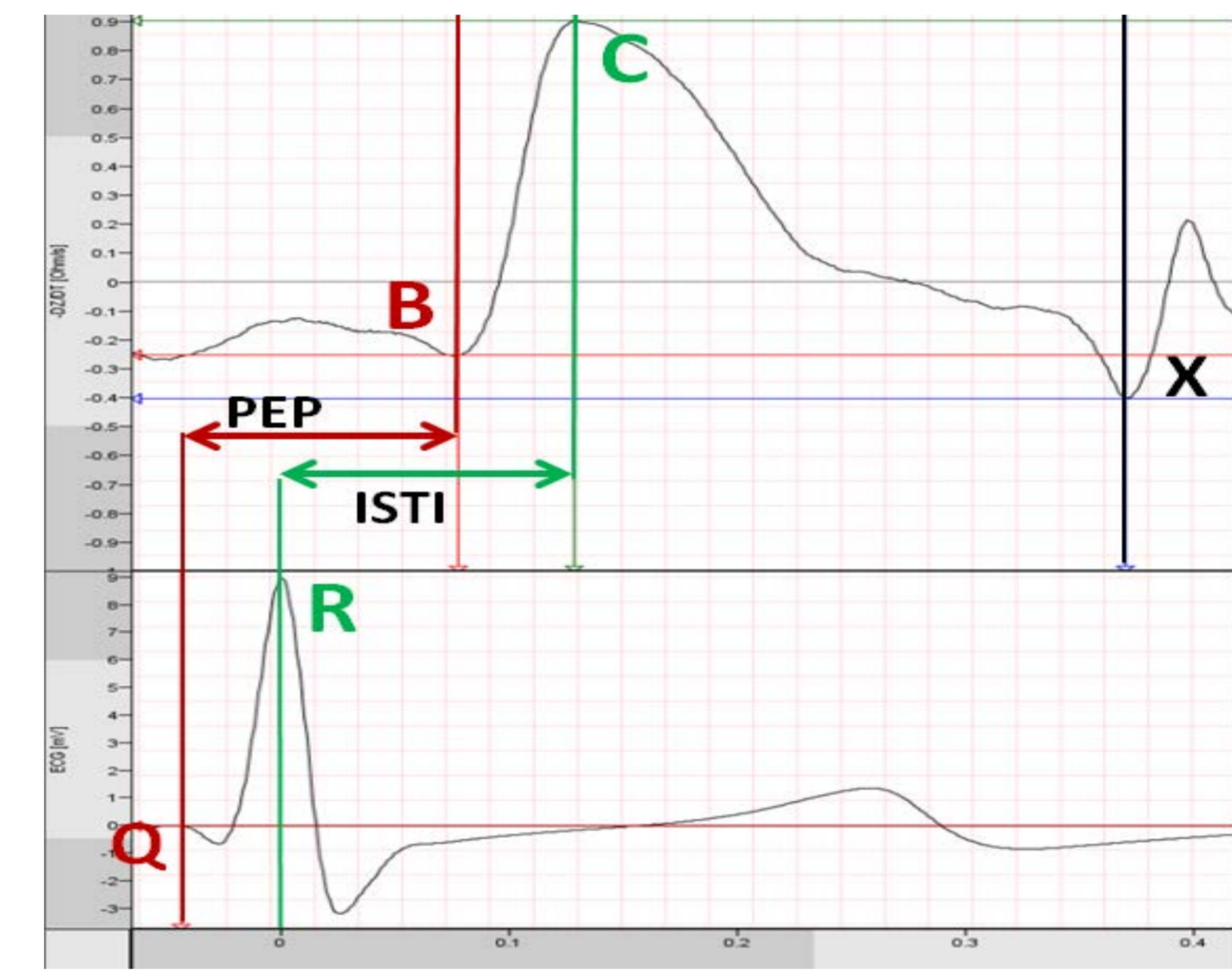
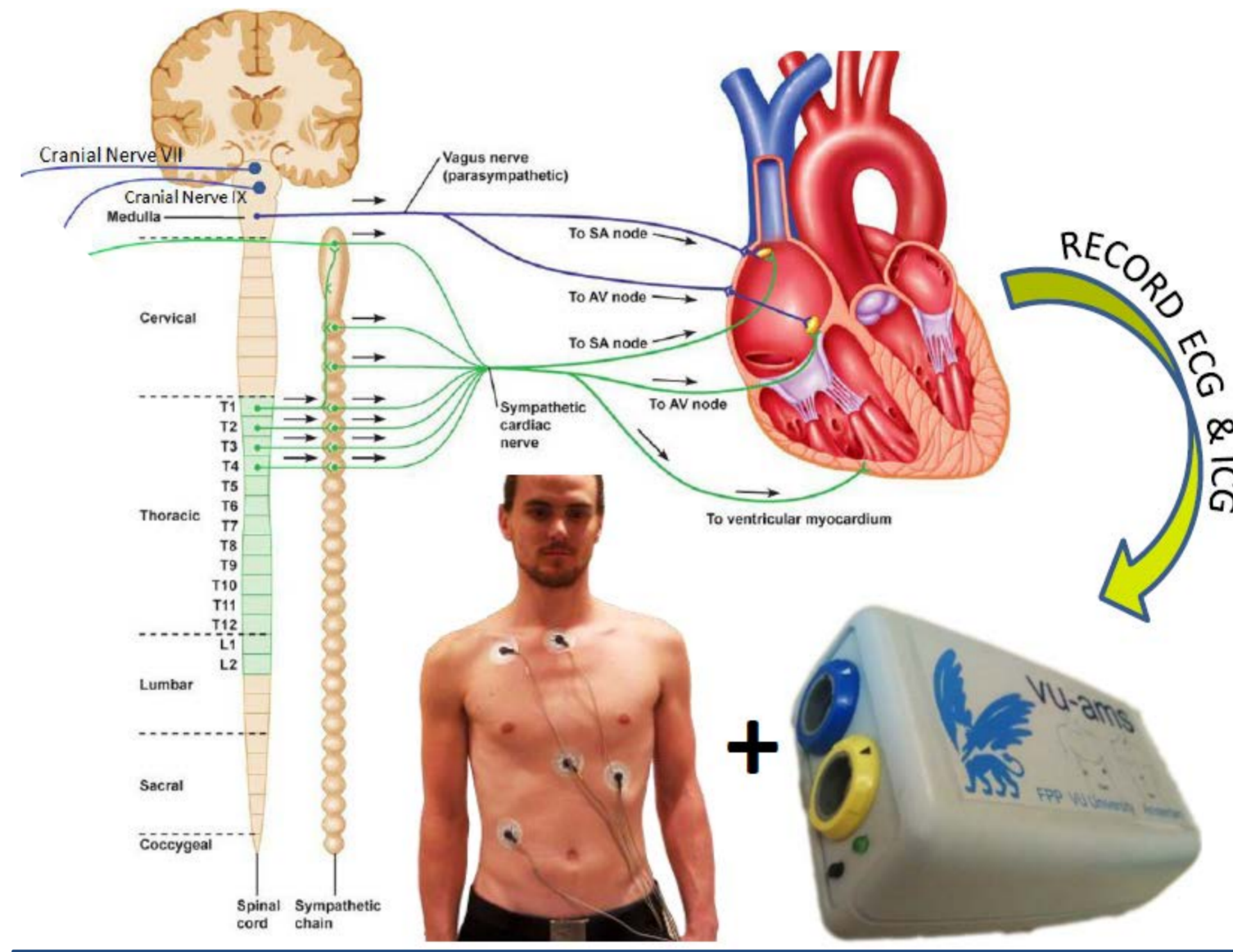


Figure 3. The Impedance Cardiogram (TOP) represents the mechanical activity of the heart and indicates the opening of the aortic valve (B-point) and the moment of maximum velocity of aortic blood flow (C-point). The Electrocardiogram (BOTTOM) represents the electrical activity of the heart and indicates the onset of the electrical activity through the heart (Q-wave onset) and the peak of electrical activity (R-wave peak). PEP is defined as the Q-wave onset to B-point interval and ISTI is defined as the interval from the R-wave peak to the C-point.

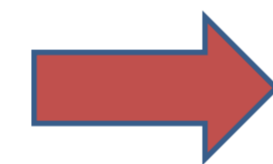
Figure 2. The ICG and ECG signals were continuously recorded with the Biopac data acquisition system (lab study) and with the VU Ambulatory Monitoring System (ambulatory study). Four landmarks were automatically scored in the electrocardiogram (ECG) and impedance cardiogram (ICG) and rigorously checked by interactive inspection of two independent raters: Q-wave onset, R-wave peak, B-point, and C-point (dZ/dt-min) (Figure 2).

Figure 1. Experimental conditions in the laboratory (N=91 (M=20/ F=71) / AGE: 21.7 (3.2) / BMI: 22.2 (2.9)) and guided ambulatory study (N=31 (M=11/ F=20)/ AGE: 22 (1.9) / BMI: 23.4 (4.3))

Statistical Analyses

QR interval VS fixed QR

The grand averaged QR interval across all subjects and all laboratory and ambulatory conditions was used to compute a weighted average QR across both studies to be used as a fixed QR interval. To test whether the QR interval can be approximated by a fixed interval the actual QR values were compared to the grand weighted average to determine the absolute agreement and its error values across both studies.



Results

The mean QR interval across all conditions was 39 ms (sd = 8 ms) in the laboratory study and 42 ms (sd = 6 ms) in the ambulatory study. The weighted grand average QR interval of both studies of was: $((39 * 91) + (42 * 31))/122 = 40$ ms. The 95% confidence interval (-14.5 ms – +14.5 ms) was found to be substantial (see Figure 4).

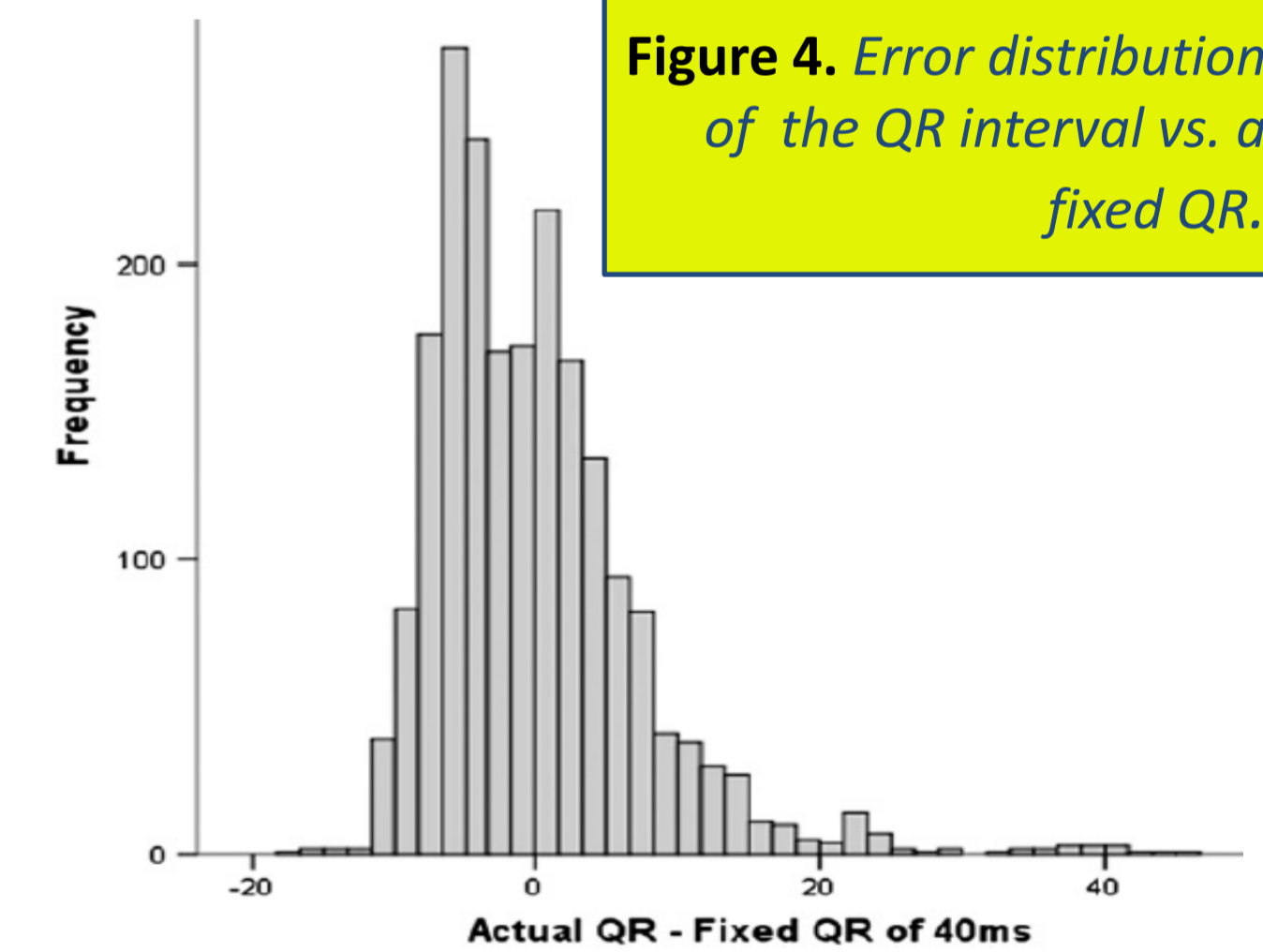
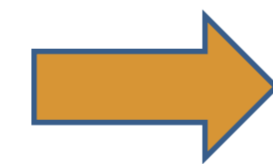


Figure 4. Error distribution of the QR interval vs. a fixed QR.

Estimation of the R-wave peak to B-point interval using the ISTI

Multilevel regression was applied to establish the optimal regression equation to predict the RB interval from the ISTI for both studies separately.



The best model to describe the relationship between the RB interval and the ISTI in the laboratory study was the extended linear model with a random intercept and a random slope, $RB = -46 + (0.9 * ISTI)$ ms and explained 79 % of the total variance in the RB interval.

Absolute agreement between actual PEP and estimated PEP

Finally, the PEP was estimated for each individual in every condition in both studies by summing the weighted grand averaged QR interval across both studies to the RB interval estimated from the ISTI using the slope and intercept parameters from the best fitting model of the laboratory study, with the ambulatory data acting as the confirmatory set. A Bland-Altman analysis was used to test the absolute agreement between the estimated PEP and the measured PEP for both studies.



Figure 5 depicts the crucial test whether the estimated PEP adequately reflects the measured PEP across a wide range of laboratory and ambulatory conditions. **PEP was estimated as: $40 + (-46 + (0.9 * ISTI))$.** The mean difference between the measured PEP and the estimated PEP in the *laboratory study* was +8 ms, and in the *ambulatory study* -4 ms. The 95% confidence intervals were very large, ranging from -20 to +36 ms for the laboratory study and from -25 to +18 ms in the ambulatory study.

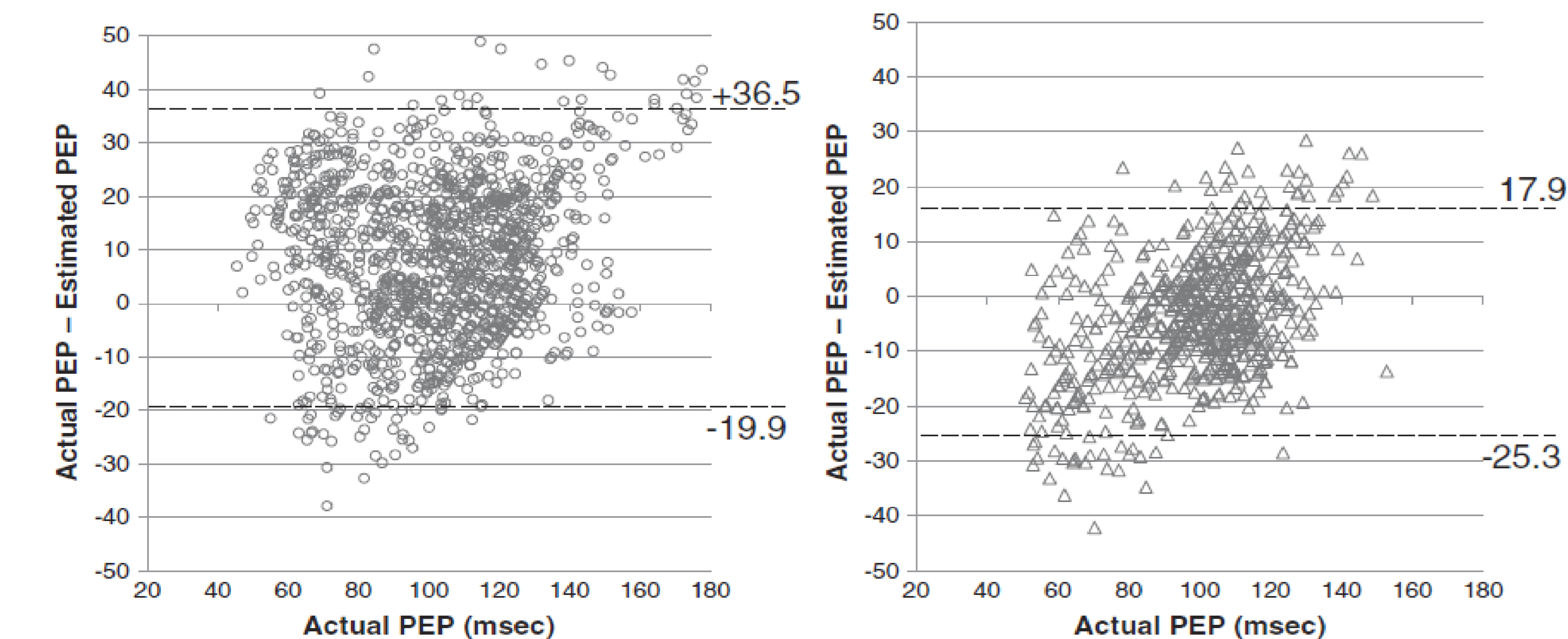


Figure 5. Scatter plots of the relationship between PEP and ISTI for the laboratory study (LEFT) and the ambulatory study (RIGHT). Note that these plots contain both within and between subject variance.

CONCLUSIONS:

For valid PEP scoring the detection of the Q-wave onset and B-point remains mandatory.

PEP estimated from the R-wave and dZ/dt-min peaks should not be used to replace the actual PEP, but could be a useful in helping to locate the Q-wave and B-points.

Focusing the detection algorithms in a window around these expected locations can assist automated detection and reduce the effort of visual inspection

