Transfer function and biosignal analysis

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Abstract: *On the example of the baroreflex sensitivity the problems of transfer function in biosignal analysis are presented. Mentioned is missing standardisation, big variety of methods and supposed definitions, and missing optimization of the diagnostic contribution.*

Introduction

The coupling between two biosignals is sometimes used as a parameter in clinical diagnosis. On example baroreflex sensitivity (BRS), the coupling between heart rate interval (R-R) and systolic blood pressure (SBP), is used as a marker in cardiology. In technical areas the coupling is given by the transfer function and the more detailed specification may be only: system is linear/nonlinear; static/dynamic. In the area of biosignal the measured system is more complex and so simple definition is mostly missing. The definition is substituted by the used method of measurement and processing. At BRS exist big variety of methods and the resulting parameter evidently depends on the method used. Missing standardization, big variety of methods and a low diagnostic contribution are reasons why BRS is often discussed in articles (more than 60 journal articles per year). But the articles mostly only compare the statistical results and do not analyze how and why to use some method of measurement or processing. In this contribution we would like to pick out some points, that are omitted.

Measurement method

The used methods can be divided according to measurement protocol, physiological aim and according to reproducibility. The categorization according to measurement protocol is commonly used and the methods are divided to two main groups [1-3]:

- Excitation by an event as: application of vasoactive drugs (phenylephrine or nitropruside); Valsalva maneuver; neck suction or lover body negative pressure test.
- Continual measurement of fluctuations of SBP and R-R with defined conditions of measurement (body and leg position, breathing, etc.)

The categorization according to physiological aim is rather hidden and is remarkable only from reasons why some authors prefer some methods again others. SBP and R-R are two signals from very complex neurovegetative system with many other input and output signals and couplings among them. Some authors suppose that BRS should be a pure coupling of baroreflex feedback system (BFS), without any other interaction. In this case no excitation can be used, because any excitation increases the influence of other couplings. But without excitation the spontaneous fluctuations of SBP and R-R are too weak and the measurement is not reproducible. So the second approach, supposed BRS as the coupling between SBP and R-R at given conditions of measurement which reflect an amount of other biological coupling, is better. This second approach is sometimes portrayed in parameter description as open loop measurement (application of vasoactive drug) or overestimated BRS (if the breathing 0.1 Hz is used).

Reproducibility of measurement. The good reproducibility should be the main prerequisite of any clinical parameter. If the reproducibility is poor, then even if the underlying physical variables are perfectly correlated, the measured correlation coefficient

and corresponding clinical contribution are low [4]. The articles mostly describe the measurement of BRS at healthy persons, where the strong coupling between SBP and R-R should be. At patient even the "gold standard" (invasive methods with application of vasoactive drugs) has a low reproducibility. Only if the breathing with frequency 0.1 Hz is used as an excitation, the reproducibility is good [5].

Processing algorithms

At the excitation by event the time domain is analyzed and BRS is computed as the linear regression slope of SBP and R-R [5,6]. The excitation is mostly applied more times and the final result is the mean level of more tests. Only empirical recommendations exist about needed minimal changes of SBP and R-R at which the test is supposed as a successful. The basic delay, with them the change of SBP is followed by change of R-R, the start and the end point of the changes are not sufficient defined too. According to algorithm, the linear static system is supposed without more detailed definition. In reality the system is not static and significant delay exist between SBP and R-R changes. The resulting BRS can vary according to used filters, basic delay and the choose of starting and end point and this parameters are not sufficient defined.

In the case of continual measurement the analysis in the time domain or in the frequency domain may be used [5,6]. The time domain analysis is called sequence method. At this method the sequences are identified in which SBP and R-R concurrently increased or decreased over three or more beats. In this sequences the linear regression slope is computed and BRS is the mean level of all sequences. Again exist empirical parameters as: minimal change of SBP and R-R to use the sequence; minimal correlation between SBP and R-R to use the sequence; basic delay between SBP and R-R changes; and minimal number of sequences to count the measurement as successful. The result and success rate depend before all on basic delay (may be from 0 to 3 beats). The minimal length of sequence (3 beats) give some information about supposed frequency area – the period is at least 6 beats, i.e. the supposed frequency is lower than 0.16 Hz. The mean length of sequences is according to our experience round 4.5 beats and this good correspond with frequency 0.1 Hz, where the maximal gain of fast circulation control should be.

In frequency domain can be used three different algorithms: transfer function; alfa index; complex demodulation. All algorithms suppose band pass signal, but the frequency bandwidth is not clear defined. The used bandwidth can be: low frequency band (LF) from 0.05 to 0.15 Hz; the band more close round 0.1 Hz; high frequency band (HF) from 0.15 to 0.4 H; the band round the respiration frequency; and the band round the frequency, where the maximal coherence between SBP and R-R exist. Again some empirical parameter (minimal coherence in analyzed frequency band) is used to count the measurement as a successful. The alpha index technique compute BRS as a square rooted ratio of R-R and SBP powers in given frequency band. The result of complex demodulation is the immediate gain that describe the dynamic behavior of circulation control and mean level of immediate gain that correspond to standard parameter BRS.

Disregard points

Different hydrostatic conditions, given by body and legs position, can change the resulting level of BRS at least two times. They change also the coupling among SBP, R-R and other signals, so the results with different body positions is not possible to compare.

The other question is, if the unit of BRS [ms/mmHg] was proper chosen. BRS as a marker in cardiology should describe the quality of circulation control, so the marker should correspond to the stability of blood flow. In this case the unit [1/(mmHg*ms)] should be better

and the coupling between SBP and heart rate should be measured. SBP is according to physiological conditions independent variable.

The last but not least question is, if the standard parameter BRS, as the mean level of gain from continuous measurement or the mean gain from more excitation can express the quality of circulation control. According to our opinion not. Only the detailed description of dynamic behavior of circulation control, given partly by immediate BRS gain, but before all by immediate phase between SBP and R-R can give the information about stability of circulation control.

The phase stability as a marker of fast circulation control

We are using the measurement (blood pressure, ECG, breathing) in supine position with controlled breathing 0.1 Hz. This breathing preserve us the determined conditions of measurement and the best and simplest excitation of baroreflex feedback system (BFS), that should have the maximal gain in this area. On the other hand we do not measure the pure influence of BFS. The SBP, R-R and breathing are three signals of neurovegetative system, among them strong couplings exist and we measure the result of this three couplings.

We compute all standard numerical parameters, given by different algorithms and parameters of processing. But as a main parameter we used the graphic presentation of SBP and R-R coherency in the LF band (from 0.05 to 0.15 Hz). The coherency is given by the stability of immediate phase of the transfer function between SBP and R-R and by the regularity of XYt graph [7-9].

Discussion

In the area of biosignals the model of system is mostly very complex, nonlinear and nonstacionar. Even if the theoretical knowledge about system and different couplings exist, it is mostly not possible to measure exact parameters of model at clinical tests. The measured signals are weak, overlapped by others coupling. The exact measurement is possible only at experimental tests on animals. So the clinic parameters are always some simplification, but important is, if the simplification is good defined and if the resulting parameter has significant diagnostic contribution. This is not the case of standard parameter BRS according to our opinion.

The level of BRS has no sense without detailed description of used method and used parameters. This is given by a big number of used methods of BRS measurement and processing. It can be stated that the mean value of BRS, obtained from defined group of measured subjects, depends not only on the selection of that group, but also on: measurement method; used algorithm; and definition of success of measurement.

The variety of methods may be greeted by peoples that like to write but not by clinic that urgently calls for diagnostic parameters. It is so simple to do some measurement and made the statistic to compare different methods. But such articles give only little scientific or clinic contribution.

Without exact definition what the measured parameter should be or some “gold” standard it has no sense to discuss different processing algorithms. This can be demonstrated on the transfer function algorithm comparable to alfa index method. According to system description the transfer function algorithm should be better and it had been used before alfa index. But according the statistical results, the alfa index should be more promising marker. It has sense and must be done to discuss the parameters of processing algorithms, as basic delay between SBP and R-R or the frequency bandwidth.

The good reproducibility and success rate of measurement are the most important property of any measurement. They are more important than the pure (according to BFS), but not reproducible, results. So the measurement with breathing 0.1 Hz, that describe the fast

circulation control including the mechanical control given by breathing, is better than the measurement with other breathing frequency.

The circulation control system is the discreet system (timing is irregular, given by heart beats), it should be nonlinear and probably nonstationar. More couplings and feedback loops exist there. The stability of such system can be hard described by mean level of coupling between two main signals (SBP, R-R). Even the immediate gain or time dependent BRS is not sufficient. The stability is much better described by the stability of the phase shift between SBP and R-R fluctuations. Phase analysis can explain some clinical paradox, as low risk of sudden cardiac death at low value of BRS and vice versa.

Conclusion

In this article we choose BRS to pick out some specific problems of biosignal measurement and processing. Comparable to technical areas this differences exist:

- The exact definition what should be the result and what and how to measure and process is mostly missing.
- The theory is sometimes underestimated (transfer function algorithm comparable to alpha index algorithm or not defined parameter of processing) and in some other cases overestimated (emphasis on pure coupling of BFS not looking on the reproducibility and success rate)
- The clinical parameters are given historically before all, without more deeper theoretical analysis (the mean gain is used and the phase fluctuation is neglected)
- It does not exist simple and fast proof of new methods and parameters. The proof is always limited by the needed amount of data and by the needed time length of survey. The results must be always statistical compared. This call for international data basis and the exchange of data.

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