New measures for assessment of impaired cerebral autoregulation

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NEW MEASUREMENTS FOR ASSESSMENT OF IMPAIRED CEREBRAL AUTOREGULATION USING NEAR-INFRARED SPECTROSCOPY

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Abstract: Some preterm infants have poor cerebral autoregulation. The concordance between cerebral intravascular oxygenation (HbD), computed as the difference between oxygenated (HbO_2) and deoxygenated (Hb) haemoglobin, and mean arterial blood pressure (MABP) reflects impaired autoregulation. As HbD is not an absolute value, we developed mathematics to prove that the cerebral tissue oxygenation (TOI), an absolute signal computed as the ratio of HbO_2 to total haemoglobin ($Hb+HbO_2$), may replace HbD. In the meantime, we attempt to theoretically predict the true level of autoregulation of a patient by defining a critical percentage of the signal recording time (CPRT). 20 preterm infants with need for intensive care were studied in the first days of life. HbD and TOI were obtained with the NIRO-300 (© Hamamatsu, Japan). Invasive MABP was measured continuously. All mathematics showed a strong similarity between HbD and TOI.

1. INTRODUCTION

The most important forms of brain injury in premature infants are partly caused by disturbances in cerebral autoregulation, the mechanism which limits cerebral blood flow (CBF) variation over a range of cerebral perfusion pressures. Autoregulation may be absent not only in sick preterm infants, but also in those that are clinically well, and there is also evidence that CBF is independent of MABP over a wide pressure range in preterm infants, suggesting that autoregulation may actually be effective in the immature brain.

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As HbD reflects CBF, autoregulation can be measured by studying the concordance between HbD and MABP, assuming no changes in oxygen consumption, in oxygen saturation and in blood volume.[1] As HbD is unfortunately not an absolute value, we focused our attention on TOI, another absolute-valued signal. We explored the relationship between HbD and TOI to prove that TOI can also be used to assess impaired cerebral autoregulation in neonates. We developed for this purpose three similarity measurements based either on a correlation coefficient between two curves, or on a multiple linear regression using least squares. However, there are some other differences between the HbD and TOI signals… In terms of the physiology the TOI reflects oxygen saturation mostly in the cerebral venous compartment. Assuming constant cerebral metabolic rate for oxygen, changes in cerebral venous oxygen saturation will parallel variations of CBF according to the Fick principle. On the other hand the HbD signal reflects the mismatch between HbO_2 and Hb. In terms of the near-infrared algorithm the TOI calculation is based on spatially resolved spectroscopy (SRS) whereas the measurement of HbD is based on the modified Beer-Lambert law assuming a path length factor. The two methodologies also happen to have different depth resolutions.

The direct concordance (DiCo) between HbD and MABP has in the literature been studied, in the field of near-infrared spectroscopy, mostly by means of the correlation (COR) and coherence (COH) coefficients, the latter one measuring the degree of linear dependence between the frequency spectra of two signals. In 2000, Tsuji et al.[1] applied COH to detect impaired cerebral autoregulation from continuous measurements. In 2001, Morren et al.[4] pursued Tsuji's work using the same methodology. Recently, Soul et al.[5] further optimized COH for continuous MABP and HbD. The partial coherence (PCOH) coefficient also measures the degree of linear dependence -in the frequency domain- between two signals, but after having eliminated in a least squares sense the contribution of other influencing signals.[2]

The above defined DiCo scores are not handy enough for the physician to handle with. Because of time variability resulting from the continuous nature of the measurements, the DiCo score value describing the infant's cerebral autoregulation differs from one time instant to another one during the recording. Therefore, we define here a measurement that synthesizes the level of autoregulation of a patient for the whole recording time. During the last years, some authors derived mathematics to synthesize in a single parameter the level of autoregulation of a patient. So did Tsuji et al.[1] when computing the mean COH of each patient for fixed periods of time. The higher this mean DiCo score, the worse the cerebral autoregulation of the patient. Last year, Soul et al.[5] proposed a pressure-passive index (PPI): dividing first the signal recordings into consecutive epochs of constant duration,[4] they computed the percentage of epochs with significant low-frequency COH between MABP and HbD. If the mean COH was higher than a certain threshold value, then score 1 was assigned to the considered epoch, otherwise it received score 0. In this paper, we defined a similar parameter called CPRT, also based on the previously presented DiCo scores.

2. DATASETS

From 20 premature infants with need for intensive care, MABP, SaO_2 (arterial oxygen saturation), HbD, and TOI were measured simultaneously at the University Hospitals Leuven in the first days of life. The babies were characterized by a mean PMA

of 28.7 weeks (24-39) and a weight ranging from 570 to 1470g. The recording time ranges from 1h30 to 23h35. The data were recorded at a sampling frequency of 100Hz by a data acquisition system Codas (CODAS©, Dataq Instruments, USA) and stored on a PC. MABP (assessed by intravascular catheterization) and SaO_2 (assessed by pulse oximetry) are analog and were digitized afterwards by the CODAS-system. The NIRO-300 signals are digital with a sampling rate of 6Hz. They were converted to analog signals with a sample-and-hold function before their introduction in the CODAS-system. From this 100Hz data, the average values for non-overlapping 5-seconds intervals were calculated (0.2Hz). This sampling frequency is still high enough, since major physiological importance can be attributed to the frequency band of 0-0.01Hz (i.e. changes occurring over several minutes).[1] The differential path length taking into account the scattering of the infrared light into the brain was set at 1.39 as commonly accepted in the literature, and encoded into the PC as a constant value.

3. METHODS

3.1. Direct Concordance Methods

We applied the COR, COH and PCOH DiCo methods. We described them previously.[3] COR was scaled such that its value matches the interval [0,1] instead of [-1,1]. In this way the COR score may be more easily compared with the ones obtained with the other methods. Before computing COR, the signals were low pass filtered to the frequency range of 0–0.01Hz.[1] We based our work on computing COH using the Welch's method as Morren et al.[4] described it. The average of COH over the frequency band of interest (0–0.01Hz) was used as DiCo score for the considered signal duration.[1,3-5] Since the concordance between the signals might vary as a function of time, a sliding window approach was used (the DiCo scores were calculated over 30-minute epochs).[4] Before applying COH and COR, we first filtered all signals to keep only the recording intervals during which the variation in SaO_2 around its mean did not exceed 5%.[3] In this way the condition of constant SaO_2 was satisfied. This procedure was not followed for PCOH, as SaO_2 was the signal of which we took off the influence on MABP and HbD/TOI. For further information on the operating conditions, we refer the reader to the literature.[3, 4] It is important to recognize here the potential limitations of the use of correlation and transfer function analyses to investigate moment-to-moment autoregulatory mechanisms, as these approaches assume a linear and stationary relationship between the signals HbD/MABP or TOI/MABP. This approach can produce misleading results in a system with non-linear and non-stationary properties.

3.2. The CPRT: A Synthesized Measurement of Cerebral Autoregulation

The acronym CPRT stands for critical percentage of the recording time, i.e. the percentage of the recording time during which the DiCo score is greater than a fixed value, called critical score value (CSV). In this work the CSV will be set by default at half the maximum DiCo score value (i.e. 0.5). In contrast to the PPI, the CPRT is not computed from boolean scores over epochs -which means a loss of accuracy-, but from the DiCo scores. As seen previously, the DiCo scores are proportional to the

autoregulation impairment. The proposed definition is moreover not limited to COH, but is applicable to all existing methods. We define the CPRT as

$$CPRT = \frac{\sum_i t_i}{t_{total}} \times 100$$

where the t_i's represent the durations of the parts of the DiCo score curve lying above the CSV, and t_{total} is the total recording time.

3.3. Similarity Measurements

The first similarity measurement computes the correlation between the interpolated DiCo score curves (CBS) related to both signals. These are the curves of the time-varying DiCo scores[3, 4] computed from MABP and HbD, and from MABP and TOI. As the CBS holds only for one infant, it has to be computed for all infants, afterwards a mean of the obtained CBSs (mCBS) is computed for each DiCo method.

The second one is based on the CPRT definition, and is done at the patient group level from the CPRTs. Figure 1 illustrates the CPRTs for all patients and for each DiCo method. For each DiCo method, we then computed a correlation coefficient between the interpolated curves related to signal sets MABP/HbD and MABP/TOI (CB-CPRT).

The last way to look at the similarity between HbD and TOI was achieved by computing a multiple linear regression, using least squares, from the mean DiCo scores of all patients (see Fig. 2). On the x-axis and y-axis, we considered the mean DiCo scores related to signal set MABP/HbD, and MABP/TOI, respectively. We used two parameters to assess the regression efficiency. The first is the mean of the absolute values of the regression residuals r_i defined as

$$\left|\bar{r}\right| = \frac{\sum_{i=1}^{n} \left|r_i\right|}{n}$$

where n is the number of patients. The second parameter is the regression mean squared error (MSE), which is an estimator of the variance of the random disturbances.

4. EXPERIMENTAL RESULTS AND DISCUSSION

The mCBS is equal to 0.76 for COH, 0.63 for COR, and 0.70 for PCOH. The CB-CPRT is equal to 0.81 for COH, 0.71 for COR, and 0.78 for PCOH (see Fig. 1). A larger follow-up study is however needed to evaluate statistically the CPRT efficiency with respect to the infant clinical outcomes. As a scaled correlation coefficient belonging to interval [0,1] was considered to compute mCBS and CB-CPRT, the obtained results are very positive.

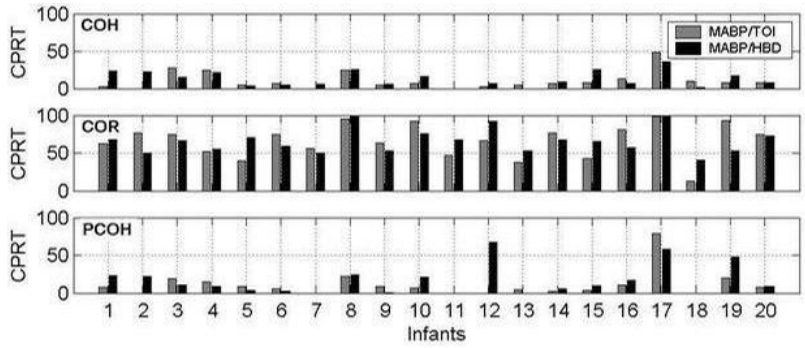


Figure 1. Illustration of the CPRTs related to each infant and for each score. For each DiCo method, a correlation coefficient (the CB-CPRT) was then computed from the interpolated CPRT curves related to both signal sets: it is equal to 0.81 for COH, 0.71 for COR, and 0.78 for PCOH.

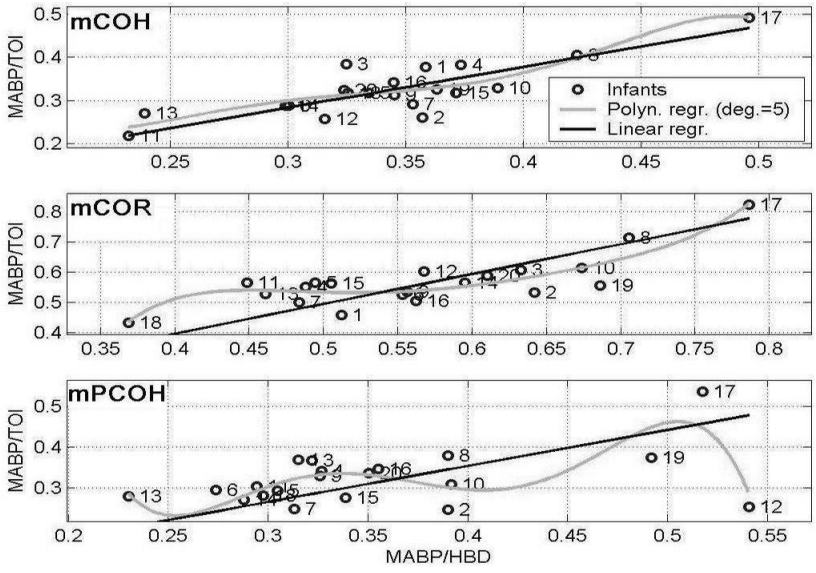


Figure 2. Multiple linear regression using least squares, achieved from the mean -over time- DiCo scores (mCOH, mCOR and mPCOH) of all patients. On the x-axis we considered the mean DiCo scores related to signal set MABP/HbD, and following the y-axis the ones of signal set MABP/TOI. The mean of the absolute values of the residuals is 0.027 for COH (corresponds to 2.7% of the full interval width [0,1] in which the DiCo scores belong), 0.043 for COR (4.3%), and 0.041 (4.1%) for PCOH. The MSE is 0.0013 for COH, 0.0031 for COR, and 0.0038 for PCOH. The figure also shows a polynomial regression of degree 5 of the data.

The mean of the absolute values of the residuals r_i is 0.027 (corresponds to 2.7% of the full interval width [0,1] in which the DiCo scores take their values) for COH, 0.043 (4.3%) for COR, and 0.041 (4.1%) for PCOH (see Fig. 2). The MSE is 0.0013 for COH,

0.0031 for COR, and 0.0038 for PCOH. The linear regression shows thus that TOI is similar to HbD as the regression parameters are low. Please see Table 1 for all results.

Table 1. Similarity measurements for proving that the behavior of TOI is similar to the one of HbD regarding cerebral autoregulation. They are based either on a correlation coefficient between two curves (CB-CPRT and mean CBS), or on a multiple linear regression using least squares (MSE and mean of |r|).

	mCBS	CB-CPRT	Mean of |r|	MSE
COH	0.76	0.81	0.027	0.0013
COR	0.63	0.71	0.043	0.0031
PCOH	0.70	0.78	0.041	0.0038

5. CONCLUSION

First, the measurements presented to study the similarities between signal sets MABP/HbD and MABP/TOI show very positive results, which brings us to claim that TOI may be used for the calculation of cerebral autoregulation in neonates. Secondly, a new synthesized measurement of cerebral autoregulation -the CPRT- was presented. In opposition to previously defined measurements, it is applicable to all existing DiCo methods, and generates a measurement of the autoregulation impairment proportional to the time-varying DiCo score between the signals of interest.

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