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Oxygen Transport to Tissue XXXI

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The Partial Coherence Method for Assessment of Impaired Cerebral Autoregulation using Near-infrared Spectroscopy: Potential and Limitations

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Abstract The most important forms of brain injury in premature infants are partly caused by disturbances in cerebral autoregulation. As changes in cerebral intravascular oxygenation (HbD), regional cerebral oxygen saturation (rSO_2), and cerebral tissue oxygenation (TOI) reflect changes in cerebral blood flow (CBF), impaired autoregulation can be measured by studying the concordance between HbD/rSO_2/TOI and the mean arterial blood pressure (MABP), assuming no changes in oxygen consumption, arterial oxygen saturation (SaO_2), and in blood volume. We investigated the performance of the partial coherence (PCOH) method, and compared it with the coherence method (COH). The PCOH method allows the elimination of the influence of SaO_2 on HbD/rSO_2/TOI in a linear way. We started from long-term recordings measured in the first days of life simultaneously in 30 infants from three medical centres. We then compared the COH and PCOH results with patient clinical characteristics and outcomes, and concluded that PCOH might be a better method for assessing impaired autoregulation.

1 Introduction

In this study in preterm infants, NIRS is used to measure cerebral autoregulation over long periods, reflecting *static autoregulation*. The use of NIRS for this purpose was described by Tsuji et al. [1]. Changes in HbD, rSO_2, or TOI reflect changes in CBF and the correlation between MABP and HbD/rSO_2/TOI is a reflection of autoregulation. A good correlation was found between autoregulation and outcome, i.e. frequency of severe intraventricular bleeds. rSO_2 and TOI are both absolute values, they are less prone to movement artefacts than HbD, and easier to measure in clinical practice.

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We studied the concordance between HbD/rSO_2/TOI and MABP by means of the coherence (COH, measuring the degree of linear dependence between the frequency spectra of two signals), and partial coherence (PCOH) [2] coefficients. The latter allows the elimination of the linear influence of one signal on another one. This means that, in contrast to COH, PCOH can also be applied in periods of fluctuating SaO_2 thereby improving the automation and the use of the method. We developed and investigated four PCOH algorithms fixing the physiological interactions between SaO_2, MABP, and HbD/rSO_2/TOI. We studied the PCOH properties, in particular during periods of fluctuating SaO_2. For this purpose we used parameters that synthesize patient level of autoregulation: the mean score (*mCOH* and *mPCOH*) [1], the pressure-passive index (*PPI*) [3] and the critical percentage of the recording time (*CPRT*) [4]. Finally, we compared these parameters with the infant clinical characteristics and outcomes: infant post menstrual age (PMA, in weeks), birth weight (BW, in g), Bayley's psychomotor (PDI) and mental (MDI) developmental indices after 9, 18, and 24 months (for the Leuven, Zurich, and Utrecht data respectively), Griffith developmental index (combination of a mental and psychomotor test) after 24 months, and APGAR score at birth and 5 min after birth.

2 Datasets

Thirty premature infants with need for intensive care were monitored, of whom 10 were from the University Hospital Zurich (Switzerland), 10 from the University Medical Centre Utrecht (The Netherlands), and 10 from the University Hospital Leuven (Belgium). SaO_2 was measured continuously by pulse oximetry, and MABP by an indwelling arterial catheter. Transcranial NIRS signals HbD (measured by the Critikon Cerebral Oxygenation Monitor 2001), rSO_2 (INVOS4100, Somanetics Corp.), and TOI (NIRO300, Hamamatsu) were measured for non-invasive monitoring of cerebral oxygenation. The signals were measured simultaneously in the first days of life. For the Zurich data, the babies were characterized by a mean PMA of 28 1/7 weeks (*std* = 2 1/7) and a mean BW of 1198 g (*std* = 439). For the Utrecht data, the babies were characterized by a mean PMA of 29 2/7 weeks (*std* = 1 2/7) and a mean BW of 1130.67 g (*std* = 311.36). For the Leuven data, the babies were characterized by a mean PMA of 28 5/7 weeks (*std* = 3 2/7) and a mean BW of 1125 g (*std* = 503.76). HbD, rSO_2, and TOI were recorded digitally on a personal computer at a sampling frequency of 1.677, 1, and 10 Hz for the Zurich, Utrecht, and Leuven data respectively. Afterwards the signals from all datasets were down-sampled to the smallest frequency multiple of the recording frequencies i.e. 0.333 Hz (periodicity: 3 s) to ensure comparability. A pre-processing algorithm was applied to the recordings of all centres to remove signal artefacts. Each artefact point was simply deleted from the recording for each signal [3]. Among the pre-processing operations, we kept all variables within normal ranges, in particular SaO_2 in the range 80–100%.

3 Methods

Since the possible concordance between MABP and the NIRS signals varies with time, we computed COH and PCOH over successive half-overlapping epochs of duration 10, 15, and 12.5 min for the Zurich, Utrecht, and Leuven data respectively. The average of COH and PCOH over the frequency band 0.0033–0.04 Hz (corresponding to phenomena of duration in the range 25–300 s) [3] was used as score for the considered epoch. The epoch durations were computed from the calibration of the mean COH (for all patients of each centre) on the mean absolute-valued correlation coefficient (COR), to be sure that the score value of 0.5 could be considered as critical (it suggests a relation between the signals based on 50% shared variance) [5]. If *mCOH* or *mPCOH* was higher than this critical score value (*CSV*), the infant was said to have an impaired cerebral autoregulation. We built the PCOH algorithms from the supposed physiological models fixing the interactions between the measured signals as follows:

- $SaO_2 = i(SaO_2) + f(\text{MABP})$
- $\text{MABP} = i(\text{MABP}) + f(SaO_2)$
- $\text{NIRS} = i(\text{NIRS}) + f(\text{MABP}) + f(SaO_2)$

where $i(\ldots)$ represents the independent part of the signal, $f(\ldots)$ stands for *is a function of*, and *NIRS* represents HbD, rSO_2, or TOI. The algorithms are:

- PCOH1 = COH(MABP–SaO_2, NIRS–SaO_2)
- PCOH2 = COH(MABP, NIRS–SaO_2)
- PCOH3 = COH(MABP–$i(SaO_2)$, NIRS–$i(SaO_2)$)
- PCOH4 = COH(MABP, NIRS–$i(SaO_2)$)

where $COH(\ldots, \ldots)$ is the coherence computed between both signals. For all patients we studied the performances of PCOH compared to COH on a global basis, but we also looked in detail at epochs with fluctuating SaO_2 and compared the results when using extra raw (non pre-processed) data.

4 Results

When considering all patients, we saw a trend of higher *mPCOH*s as compared to *mCOH*. In addition the *CPRT*s and *PPI*s of PCOH were generally higher as compared to the *CPRT* and *PPI*s of COH. PCOH3 shows a higher *mPCOH*, *CPRT*, *and PPI* than the other PCOH algorithms, and than PCOH2 which shows the lowest values. For more details we refer to Tables 1, 2 and 3. We also considered patients for whom the oxygen fraction of the inspired air has been intentionally modified. We particularly concentrated on epochs with a high variance in SaO_2. In these epochs, mean scores were significantly higher with PCOH3 as the highest. More details are given in Table 4 and Fig. 1

Table 1 Mean score, standard deviation (*std*), critical percentage of the recording time (*CPRT*), and pressure-passive index (*PPI*) with confidence level $\alpha = 0.1$ of the Leuven data. The numbers below are averages on the ten infants from Leuven

Leuven	COH	PCOH1	PCOH2	PCOH3	PCOH4
Mean	0.39	0.41	0.41	0.44	0.42
Std	0.09	0.1	0.09	0.12	0.1
CPRT	14%	20%	14%	27%	22%
PPI10	10.64%	12.40%	11.60%	18.35%	17.02%

Table 2 Mean score, standard deviation, *CPRT*, and *PPI10* of the Utrecht data. The numbers below are averages on the ten infants from Utrecht

Utrecht	COH	PCOH1	PCOH2	PCOH3	PCOH4
Mean	0.35	0.34	0.33	0.39	0.36
Std	0.09	0.09	0.09	0.1	0.09
CPRT	13%	11%	8%	22%	17%
PPI10	20.80%	19.30%	15.10%	28.16%	21.45%

Table 3 Mean score, standard deviation, *CPRT*, and *PPI10* of the Zurich data. The numbers below are averages on the ten infants from Zurich

Zurich	COH	PCOH1	PCOH2	PCOH3	PCOH4
Mean	0.57	0.61	0.57	0.63	0.63
Std	0.09	0.1	0.09	0.12	0.12
CPRT	72%	75%	70%	80%	71%
PPI10	17.02%	34.02%	19.27%	40.06%	29.04%

Table 4 Local analysis: the oxygen fraction inhibited by the infant has, in some Zurich patients, intentionally been modified to create locally a high variance in SaO_2. The table contains the overall score means of such a patient, and the means related to the epoch of high SaO_2 variance (20–40 min). Please see also Fig. 1

Zurich	*mCOH*	*mPCOH1*	*mPCOH2*	*mPCOH3*	*mPCOH4*	*stdSaO*$_2$
Overall	0.55	0.52	0.52	0.61	0.57	1.2
20–40	0.64	0.51	0.61	0.75	0.73	2.51

mPCOH3 detects a few more patients with impaired autoregulation than do *mCOH* and the other *mPCOHs*. The *CPRT* and *PPI10* (with confidence level $\alpha = 0.1$) detects many more patients with impaired autoregulation than *mCOH* and *mPCOHs*, and approximately twice as many patients as *PPI5* ($\alpha = 0.05$).

Patients with *mCOH* and *mPCOHs* > 0.5 have a slightly lower mean PMA and BW than the overall average. High PCOH values ($m > 0.5$, $CPRT > 0$, $PPI > 0$) are better indicators of poor clinical outcome than COH (MDI < 84, PDI < 84, Apgar < 7). *CPRT* and *PPI10* are better indicators of poor clinical outcome than mean score values.

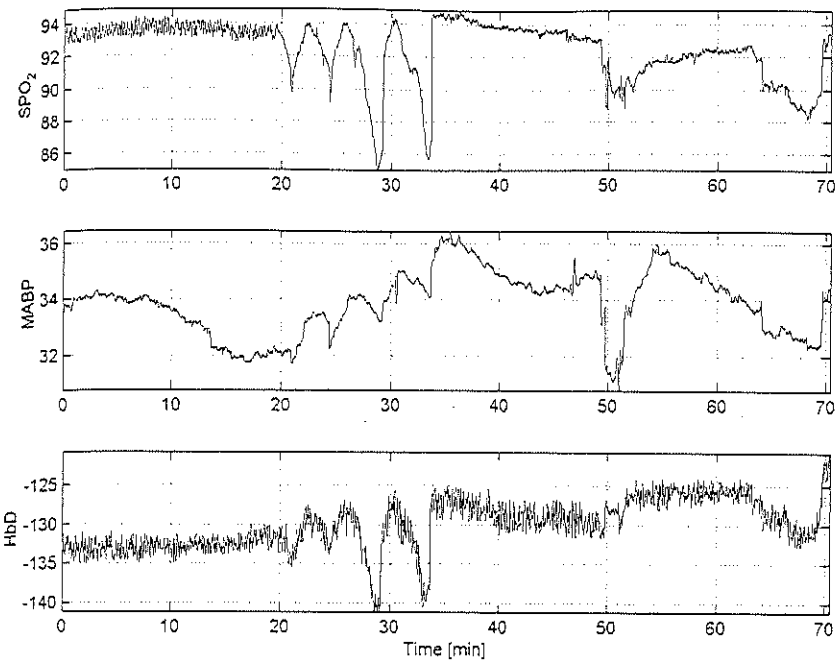

Fig. 1 Local analysis: the oxygen fraction inhibited by the infant has, in some Zurich patients, intentionally been modified to create locally a high variance in SaO_2. Please see also Table 4

5 Discussion

It is important to remember that COH and PCOH are measurements of impaired cerebral autoregulation, and that the considered clinical patient characteristics suggest possible brain damage. An evident correlation between impaired autoregulation and brain damage in neonates has been described in the literature and this is what we assume in this study. We looked for the method that best fits the occurrences of brain damage. Our results indicate that (1) the PCOH score is more accurate in detecting infants with brain malfunctions as compared to the COH method; (2) PCOH3 has the highest accuracy in detecting impaired autoregulation.

In particular, the *CPRT* and *PPI10* – computed from the COH and PCOH scores – detect more than 50% of all infants with poor clinical outcomes. These observations indicate rather that PCOH highlights more cases of impaired autoregulation as compared to COH, and does not necessarily mean that PCOH indicates a better fit between patients with impaired autoregulation and patients with poor clinical outcome. However, we should remark that in this study the patient characteristics and outcomes are not available for all

patients whereas further statistical analysis on larger multicentre datasets are needed

We expected the PCOH4 model to be more realistic than the $PCOH_3$ method, because SaO_2 was seen to have an influence on MABP only in those recordings with changes in SaO_2 which were deliberately provoked by modifying the inspired oxygen fraction. Nevertheless, this could not be confirmed by our results. Furthermore, a lack of concordance with patient neurological outcomes could also be explained by the fact that COH (and consequently PCOH) only measures the linear and stationary concordance between MABP and the NIRS-measured signals, or by the fact that PCOH assumes a linear dependency between the considered signals.

In conclusion, as $HbD/rSO_2/TOI$ are often considered as surrogate for CBF, impaired autoregulation can be assessed by quantifying the concordance between these signals and MABP. As it is able to eliminate the influence of other signals such as SaO_2, the partial coherence method was shown to perform better than the classical coherence method.

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