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Submitted to the 2008 ISOTT conference, Sapporo (Japan).
Available online at:
ftp://ftp.esat.kuleuven.be/sista/ddesmet/reports/0808-1-ISOTT.pdf

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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 cerebral intravascular oxygenation (HbD), regional cerebral oxygen saturation (rSO_2), and cerebral tissue oxygenation (TOI) reflect 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, saturation (SaO_2), and in blood volume. We investigated the performance of the partial coherence (PCOH) method, and compared it to the coherence method (COH). The PCOH method allows to eliminate in a linear way the influence of SaO_2 on HbD/rSO_2/TOI. 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, cerebral autoregulation is measured in neonates by means of near-infrared spectroscopy (NIRS) over long periods, reflecting *static autoregulation*. The use of NIRS was shown by Tsuji et al. (2000). 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 also found between

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autoregulation and outcome, i.e. frequency of severe intraventricular bleedings. rSO_2 and TOI are both absolute values, they are less prone to movement artefacts than HbD, and more easy to measure in clinical practice.

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) (Leuridan et al. 1985) coefficients. The latter one allows eliminating in a linear way the influence of one signal on another one. This means that, contrary to COH, PCOH can also be applied in periods of fluctuating SaO_2 thereby improving automation and usability 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 synthesizing the patient level of autoregulation: the mean score (*mCOH* and *mPCOH*) (Tsuji et al. 2000), the pressure-passive index (*PPI*) (Soul et al. 2007), and the critical percentage of the recording time (*CPRT*) (De Smet et al. 2008). Finally, we compared these parameters with the following -when available- 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 minutes after birth.

2 Datasets

30 premature infants with need for intensive care were monitored, among whom 10 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 oxymetry, 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 1198g (*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 1130.67g (*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 1125g (*std*=503.76). HbD, rSO_2, and TOI were digital. The data were recorded on a personal computer at a sampling frequency of 1.677Hz, 1Hz, and 10Hz for the Zurich, Utrecht, and Leuven data respectively. The signals from all datasets were afterwards downsampled to the smallest frequency multiple of the recording frequencies i.e. 0.333Hz (periodicity: 3s) to

ensure comparability. A preprocessing algorithm was also applied to the recordings of all centres to remove artefacts contained in the signals. Each artefact point was simply deleted from the recording for each signal (Soul et al. 2007). Among the preprocessing 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 minutes for the Zurich, Utrecht, and Leuven data respectively. The average of COH and PCOH over the frequency band 0.0033-0.04Hz (corresponding to phenomena of duration in the range 25-300*s*) (Soul et al. 2007) was used as score for the considered epoch. The epoch durations were computed from the calibration of the mean COH (of all patients of a center) 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) (de Boer et al. 1985). 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 $i(...)$ represents the independent part of the signal, $f(...)$ stands for *is a function of*, and *NIRS* represents HbD, rSO_2, or TOI. The algorithms are:

- $\text{PCOH1} = \text{COH}(\text{MABP} - SaO_2 , \text{NIRS} - SaO_2)$
- $\text{PCOH2} = \text{COH}(\text{MABP} , \text{NIRS} - SaO_2)$
- $\text{PCOH3} = \text{COH}(\text{MABP} - i(SaO_2) , \text{NIRS} - i(SaO_2))$
- $\text{PCOH4} = \text{COH}(\text{MABP} , \text{NIRS} - i(SaO_2))$

where $COH(\dots , \dots)$ is the coherence computed between both mentioned signals. We studied for all patients the performances of PCOH compared to COH on a global way, but we also looked more locally at epochs with fluctuating SaO_2 and also compared the results when using extra raw (non preprocessed) data.

4 Results

When considering all patients, the *mPCOHs* were most of time a bit higher than *mCOH*. Similarly the *CPRTs* and *PPIs* of PCOH were most of time a bit higher than the *CPRT* and *PPIs* of COH. PCOH3 shows a higher *mPCOH*, *CPRT, and*

PPI than the other PCOH algorithms, and than PCOH2 which shows the lowest values. Please see Tables 1 to 3. We also considered patients for whom the oxygen fraction of the inhibited air has been intentionally modified. We particularly concentrated on epochs with higher variance in SaO_2: all mean scores were significantly higher, of which PCOH3 has the highest. Please see Table 4 and Fig. 1.

mPCOH3 highlights a few more patients undergoing an impaired autoregulation than *mCOH* and the other *mPCOHs*. The *CPRT* and *PPI10* (with confidence level α=0.1) highlights much more patients with impaired autoregulation than *mCOH* and *mPCOHs*, and approximatively two times more patients than *PPI5* (α=0.05).

Patients with *mCOH* and *mPCOHs* > 0.5 have a slightly lower mean PMA and BW than that of the 30 patients. High PCOH values (*m*>0.5, *CPRT*>0, *PPI*>0) better detect bad clinical outcome than COH (MDI<84, PDI<84, Apgar<7). *CPRT* and *PPI10* better detect bad clinical outcome than mean score values.

5 Discussion

It is important to remind first that at one side COH and PCOH are measurements of impaired cerebral autoregulation, and that at the other side the considered clinical patient characteristics witness a possible brain damage. In the literature it is accepted that there is an evident correlation between impaired autoregulation and brain damage in neonates. It is what we assume in this study, even if this hypothesis is increasingly disproved by some. Consequently, we are looking at the method fitting the best occurrences of brain damage. For this purpose, using the PCOH score diagnoses more infants having brain malfunctions than if using COH, PCOH3 showing the best results. Particularly, the *CPRT* and *PPI10* -computed from the COH and PCOH scores- detect more than 50% or all infants with bad clinical outcomes. These observations are in great measure due to the fact that PCOH highlights more cases of impaired autoregulation than COH, and not necessarily that there is for PCOH a better fit between patients with impaired autoregulation and patients with bad clinical outcome. Let us also remark that in this study the patient characteristics and outcomes are not all available for each patient, a further statistical analysis on larger multicentre datasets is for this reason needed.

Secondly, we expected the PCOH4 model to be more realistic than the PCOH3 one, because SaO_2 showed to have an influence on MABP only in some recordings, wherein changes in SaO_2 were deliberately provoked by modifying the inspired oxygen fraction, but this study does not confirm this.

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 that PCOH assumes a linear dependency between the considered signals.

Finally, even if the similarity of the NIRS signals is commonly accepted, let us note that HbD is an image of the cerebral arterial compartment and that rSO_2 and TOI reflect more the venous one, each of these signals being estimated using slightly different methodologies.

Acknowledgments The research was supported by: Research Council KUL: GOA AMBioRICS, CoE EF/05/006, by FWO projects G.0519.06 (Noninvasive brain oxygenation), and G.0341.07 (Data fusion), by Belgian Federal Science Policy Office IUAP P5/22.

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Table 1 Mean score, standard deviation (*std*), critical percentage of the recording time (*CPRT*), and pressure-passive index (*PPI*) with confidence level α=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	0.11	0.1
CPRT	14%	20%	14%	27%	22%
PPI10	10.10%	12.40%	11.60%	18.30%	10.40%

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

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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%	28.20%	21.50%

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	0.56	0.61	0.57	0.63	0.59
Std	0.09	0.09	0.09	0.12	0.11
CPRT	72%	75%	70%	80%	71%
PPI10	17.00%	34.00%	19.30%	40.10%	29.00%

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 (20-40min). Please see also Fig. 1.

Zurich	*mCOH*	*mPCOH1*	*mPCOH2*	*mPCOH3*	*mPCOH4*	*stdSaO2*
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

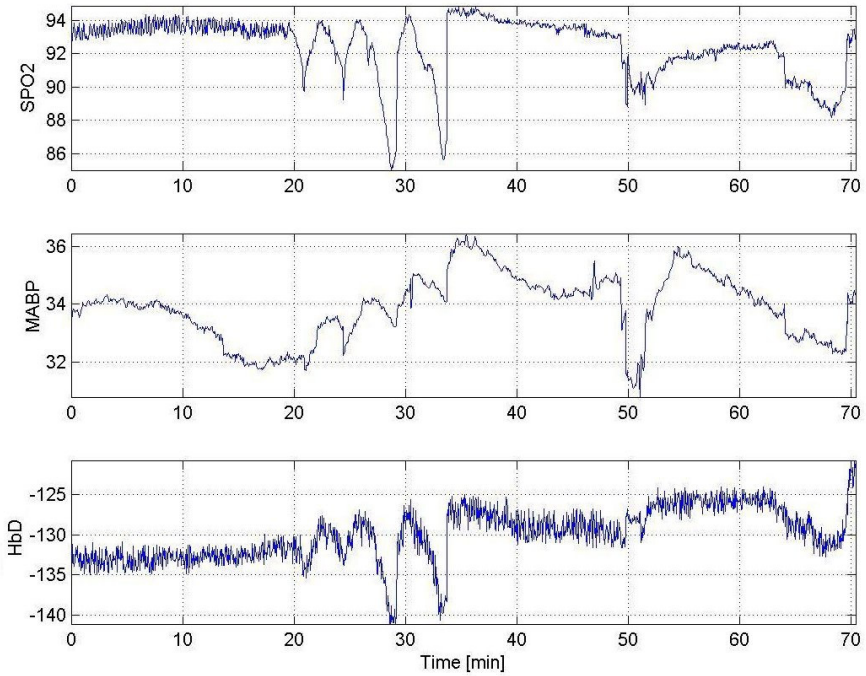


Fig. 1 Local analysis: the oxygen fraction inhibited by the infant has, in some Zurich patients, intentionally been modified to create locally a high variance in SaO_2. Please see also Table 4.