Minerva Cardioangiologica
EDIZIONI MINERVA MEDICA

Cerebral spatially resolved near-infrared spectroscopy (SRS-NIRS): paving the way for non-invasive assessment of cerebral hemodynamics during atrial fibrillation.

Andrea SAGLIETTO, Stefania SCARSOGLIO, Luca RIDOLFI, Daniela CANOVA, Matteo ANSELMINO

Minerva Cardioangiologica 2020 Mar 11
DOI: 10.23736/S0026-4725.20.05242-1

Article type: Editorial

Article first published online: March 11, 2020
Manuscript accepted: March 9, 2020
Manuscript received: March 2, 2020

Cerebral spatially resolved near-infrared spectroscopy (SRS-NIRS): paving the way for non-invasive assessment of cerebral hemodynamics during atrial fibrillation.

Andrea Saglietto[1*], Stefania Scarsoglio[2], Luca Ridolfi[3], Daniela Canova[1], Matteo Anselmino[1]

[1]Division of Cardiology, "Città della Salute e della Scienza di Torino" Hospital, Department of Medical Sciences, University of Turin, Turin, Italy;
[2]Department of Mechanical and Aerospace Engineering, Politecnico di Torino, Turin, Italy;
[3]Department of Environmental, Land and Infrastructure Engineering, Politecnico di Torino, Turin, Italy.

* Corresponding author: Andrea Saglietto; address: corso Dogliotti 14, 10126, Torino, Italy; telephone number: (39)-0116709598; fax: (39)-0112369598; email address: andrea.saglietto@live.com

Total word count:

Conflict of interests: none

Funding: This study was performed thanks to the support of the "Compagnia di San Paolo" within the project "Progetti di Ricerca di Ateneo–2016: Cerebral hemodynamics during atrial fibrillation (CSTO 60444)" of the University of Turin, Italy.

Keywords: near-infrared spectroscopy; cerebral hemodynamics; atrial fibrillation.

Current estimated prevalence of atrial fibrillation (AFib) is 1-4% worldwide, with alarming epidemiological predictions forecasting doubling of prevalence by 2050 [1]. In addition to the well-known five-fold risk of ischemic stroke [2], AFib patients are at increased risk of dementia compared to the general population, even if adequately anticoagulated and in the absence of clinical ischemic stroke [3,4]. Different concurrent mechanisms are at the basis of this stroke-independent association, such as silent cerebral ischemia [5], cerebral microbleeds [6], chronic reduction in mean cerebral blood flow [7], AFib-related inflammation [8] and cerebrovascular endothelial dysfunction [9]. In addition, beat-to-beat interval variation during AFib potentially exerts direct effects on the distal cerebral hemodynamics, but this field has seldom been clinically explored. In fact, to date, the only available data regarding the potential beat-to-beat influence of the irregular heart rhythm on the distal cerebral circle derives from a computational study, which postulated that transient critical events, such as hypoperfusions or hypertensive events, may occur during AFib in the brain tissue [10,11].

Non-invasive hemodynamic assessment of the cerebral circulation has been attempted. The most widely used technique is transcranial Doppler (TCD), which uses low-frequency (≤2 MHz) ultrasound waves to insonate the basal cerebral arteries, enabling the measurement of cerebral blood flow velocity in the major intracranial arteries with high temporal resolution [12]. However, the technique is limited by operator-dependency, assumptions made regarding vessel diameter and low spatial resolution, since it lacks the resolving power to assess hemodynamic signals downstream the proximal intracranial arteries. Another available technique is arterial spin labelling perfusion magnetic resonance imaging (ASL-MRI), which uses endogenous tracers (water protons in the arterial blood) to quantify regional cerebral blood flow. This approach permits to achieve high spatial resolution, yet temporal resolution is by far inferior to TCD. Due to this limitation, although ASL-MRI [13] is able to assess regional cerebral blood flow, the limited temporal resolution hampers beat-to-beat analysis of the distal cerebral circulation.

In this context, cerebral near-infrared spectroscopy (NIRS), a known technique to monitor deepness of general anaesthesia in surgery and critical care, holds an intriguing potential to provide unique

insights on hemodynamics of cerebral circle during AFib. This optical technique is based on the principle that light in the near-infrared (NIR) range (700 nm to 1000 nm) is able to pass through the skin, soft tissue and bone, penetrating brain tissue to a depth of up to 2 cm [14]. The computed hemodynamic signal is derived on the absorption of NIR light by haemoglobin, different according to the oxygenation state of the protein, thus permitting to quantify changes in the tissue concentration of intravascular oxygenated haemoglobin (HbO_2) and deoxygenated haemoglobin (HbH). However, even though been sensitive to cerebral microvasculature, cerebral NIRS signals are also potentially affected by extra-cranial blood from various sources (skin, subcutaneous fat, skull). This observation prompted the development of a number of techniques, such as time-resolved spectroscopy, frequency-resolved spectroscopy and spatially-resolved spectroscopy (SRS), aimed at minimizing the influence of extracerebral circulation on NIRS measurements.

SRS-NIRS, in particular, implements an algorithm based on collecting the back-scattered light from the tissue at multiple sites, which focuses the measurement on the deep rather than superficial tissues [15].

This approach provides two additional parameters: tissue oxygenation index (TOI), which is a measure of cerebral tissue oxygenation, and tissue haemoglobin index (THI), which is a measure of cerebral tissue haemoglobin concentration reflecting local changes in blood volume (assuming a constant haematocrit). Therefore, SRS-NIRS signals hold the potential to provide insights on cerebral hemodynamic signals with high temporal resolution, being potentially sensitive to beat-to-beat changes at the distal cerebrovascular level and overcoming the limitation of the previously cited techniques.

Based on these presumptions our group has run a preliminary set of acquisitions and the first analysis support the hypothesis that SRS-NIRS is able to provide beat-to-beat information on the sampled cerebral tissue during AFib. We performed NIRS cerebral monitoring lasting 4 minutes in 6 volunteers with AFib, using the NIRO-200NX device (Hamamatsu Photonics K.K., Japan), with the highest sampling frequency available (20 Hz). After appropriate filtering on the raw SRS-NIRS

signals (see Figure 1 for examples of post-processed SRS-NIRS signals), a peak detection analysis was performed to compute inter-beat intervals from TOI and THI signals, respectively. These intervals were then compared to the inter-beat intervals derived from synchronized ECG analysis, considered as gold standard. Table 1 reports mean and standard deviation of TOI-, THI- and ECG-derived inter-beat intervals obtained from all the 6 volunteers, showing no difference between the inter-beat intervals inferred from SRS-NIRS signals and ECG. Consequently, SRS-NIRS signals show the ability to intrinsically integrate hemodynamic information at the beat-to-beat level.

In conclusion, the constant rise in AFib prevalence obliges not to stop to the mere description of only the classical clinical events (death, stroke, heart failure hospitalization), since dementia and cognitive decline are subtle phenomena, potentially not preventable by oral anticoagulation therapy, the cornerstone of AFib management. Cerebral SRS-NIRS with high sampling frequency (20 Hz), a non-invasive and easily affordable technique, can provide unique, beat-to-beat hemodynamic details of the distal cerebral circulation, candidating as a significant tool to shed light on the impact that AFib exerts on brain circulation.

Acknowledgments

We would like to thank patients, Prof. Gaetano Maria De Ferrari, Prof. Mauro Rinaldi and Elisabetta Toso for participating at the study. We also thank Prof. Silvestro Roatta, Ivan Ferrandino, Nefer Gianotto and Alessandro Piccotti for helping in the setting-up of the recordings. Special mention goes to Antonietta Carfora, Elena Maria Richiardi, Anna Renzetti, Prof. Enrico Lupia, Prof. Luca Brazzi (for his group of Anesthesiologists), and Antonio Ferraro (for his group of Professional Nurses) for actively promoting the study.

References

1. Zulkifly H, Lip GY, Lane DA. Epidemiology of atrial fibrillation. International journal of clinical practice 2018; 72 (3):e13070.
2. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke; a journal of cerebral circulation 1991; 22 (8):983-988.
3. Graves KG, May HT, Jacobs V, Bair TL, Stevens SM, Woller SC, et al. Atrial fibrillation incrementally increases dementia risk across all CHADS2 and CHA2DS2VASc strata in patients receiving long-term warfarin. American heart journal 2017; 188:93-98.
4. Saglietto A, Matta M, Gaita F, Jacobs V, Bunch TJ, Anselmino M. Stroke-independent contribution of atrial fibrillation to dementia: A meta-analysis. Open heart 2019; 6 (1):e000984.
5. Gaita F, Corsinovi L, Anselmino M, Raimondo C, Pianelli M, Toso E, et al. Prevalence of silent cerebral ischemia in paroxysmal and persistent atrial fibrillation and correlation with cognitive function. Journal of the American College of Cardiology 2013; 62 (21):1990-1997.
6. Selim M, Diener H-C. Atrial fibrillation and microbleeds. Stroke; a journal of cerebral circulation 2017; 48 (10):2660-2664.
7. Lavy S, Stern S, Melamed E, Cooper G, Keren A, Levy P. Effect of chronic atrial fibrillation on regional cerebral blood flow. Stroke; a journal of cerebral circulation 1980; 11 (1):35-38.
8. Aldrugh S, Sardana M, Henninger N, Saczynski JS, McManus DD. Atrial fibrillation, cognition and dementia: a review. Journal of cardiovascular electrophysiology 2017; 28 (8):958-965.
9. Junejo RT, Braz ID, Lucas SJ, van Lieshout JJ, Phillips AA, Lip GY, et al. Neurovascular coupling and cerebral autoregulation in atrial fibrillation. Journal of Cerebral Blood Flow & Metabolism 2019:0271678X19870770.
10. Anselmino M, Scarsoglio S, Saglietto A, Gaita F, Ridolfi L. Transient cerebral hypoperfusion and hypertensive events during atrial fibrillation: a plausible mechanism for cognitive impairment. Sci Rep 2016; 6:28635.
11. Saglietto A, Scarsoglio S, Ridolfi L, Gaita F, Anselmino M. Higher ventricular rate during atrial fibrillation relates to increased cerebral hypoperfusions and hypertensive events. Scientific reports 2019; 9 (1):1-9.
12. Purkayastha S, Sorond F. Transcranial Doppler ultrasound: technique and application. Semin Neurol 2012; 32 (4):411-420.
13. Ferré J-C, Bannier E, Raoult H, Mineur G, Carsin-Nicol B, Gauvrit J-Y. Arterial spin labeling (ASL) perfusion: techniques and clinical use. Diagnostic and interventional imaging 2013; 94 (12):1211-1223.
14. Murkin JM, Arango M. Near-infrared spectroscopy as an index of brain and tissue oxygenation. British journal of anaesthesia 2009; 103 (suppl_1):i3-i13.
15. Suzuki S, Takasaki S, Ozaki T, Kobayashi Y. Tissue oxygenation monitor using NIR spatially resolved spectroscopy. Optical Tomography and Spectroscopy of Tissue III: International Society for Optics and Photonics; 1999. pp. 582-592.

Figure Legends

Figure 1. Example of post-processed TOI (green) and THI (violet) SRS-NIRS signals, together with the non-spatially resolved O2Hb signal (red).

Tables

Table 1. Mean and standard deviation of the inter-beat interval derived by SRS-NIRS and ECG signals.

Parameter	Mean	Standard deviation	*T test* p-value (comparison to inter-beat interval derived from ECG)
TOI	0.72 s	0.12 s	0.888
THI	0.73 s	0.11 s	1.000
ECG	0.73 s	0.12 s	Ref