Available online at www.sciencedirect.com

ScienceDirect

Procedia Computer Science 176 (2020) 2923–2929

Procedia Computer Science

www.elsevier.com/locate/procedia

24th International Conference on Knowledge-Based and Intelligent Information & Engineering Systems

Wireless EEG in hyper-acute ischemic stroke: correlation between neurophysiological alterations and CTP total hypoperfused volume

Miloš Ajčević[a,b,*], Giovanni Furlanis[b], Aleksandar Miladinović[a], Marcello Naccarato[b], Giulia Silveri[a], Paola Caruso[b], Agostino Accardo[a], Paolo Manganotti[b]

[a]*Department of Engineering and Architecture, University of Trieste, Trieste, Italy*
[b]*Neurology Unit, University Hospital of Trieste, Department of Medicine Surgery and Health Sciences, University of Trieste, Trieste, Italy*

Abstract

Neuroimaging is crucial for stroke diagnosis and to establish the feasibility of reperfusion therapy, but is not practical for the assessment of continuous evolution of brain ischemia. Electroencephalography (EEG) in the early phase of brain ischemia could be a feasible instrument of functional monitoring. In this context, it would be of great research and clinical interest to assess the relation between EEG parameters and the hypoperfused volume measured by Computed Tomography Perfusion (CTP), as possible real-time surrogate parameters for extent of brain ischemia. This preliminary study aimed at investigating the relation between stroke-related EEG changes, measured on bedside with wireless EEG device, and the extent of hypoperfused volume assessed on CTP during the hyper-acute phase. We studied 12 consecutive ischemic stroke patients who underwent CTP assessment and EEG recording with wireless device within 4.5 hours from symptom onset. Total hypoperfused volume correlated significantly with the delta/alpha power ratio (ρ=0.72; $p<0.010$), (delta+theta)/(alpha+beta) power ratio (ρ=0.68; p=0.018), as well as with relative delta power (ρ=0.61, $p<0.041$). A significant negative correlation was found between relative alpha power (ρ=-0.77; p=0.003) and hypoperfused volume. In conclusion, EEG could be useful for the assessment of stroke severity and functional longitudinal monitoring.

* Corresponding author. Tel.: +39-040-5587120; fax: +39-040-5583460.
E-mail address: majcevic@units.it

1877-0509
10.1016/j.procs.2020.09.261

Keywords: EEG; Wireless device; CT Perfusion; Hyperacute Ischemic Stroke; Ischemic volume;

1. Introduction

Stroke still represents one of the leading causes of serious long-term disability or death among elderly population worldwide [1]. Neuroimaging has been proving to be pivotal in diagnosis of ischemic stroke and it is of paramount importance for patients' eligibility for treatment [2-6]. Magnetic resonance imaging (MRI) and Computed Tomography Perfusion (CTP) are able to assess the extent ischemic core and salvageable hypoperfused penumbra [7]. These neuroimaging techniques can identify acute stroke patients who can most benefit from the reperfusion thrombolysis and thrombectomy reperfusion therapy [8, 9]. CTP is increasingly adopted in emergency settings especially because of its particularly fast imaging time. This neuroimaging technique also is characterized by high sensitivity (80%) and specificity (95%) [10]. Nevertheless, MRI- and Computed Tomography (CT) -based perfusion imaging techniques are not practical to monitor brain ischemia evolution during the critical hyper-acute period.

Electroencephalography (EEG) could be a feasible instrument for bedside functional monitoring in emergency setting [11]. However, performing an EEG in emergency units could be difficult due to the limited space, staff training and complexity of the equipment [12]. In this context, a portable device based on wireless technologies may overcome aforementioned inhibiting factors [13, 14] allowing its application in hyperacute phase without compromising the treatment protocol.

In stroke patients cerebral blood flow (CBF) reduction in ischemic areas cause EEG activity changes. In particular, these variations are characterized by increased power mainly in delta frequency range and decreased in alpha frequency range [11]. EEG alterations during the sub-acute and post-acute phase of ischemic stroke has been widely studied [15-17]. The spectral parameters as relative delta power [15], the delta/alpha power ratio (DAR) [15], and (delta+theta)/(alpha+beta) (DTABR) power ratio [16] have been reported as very informative for clinical outcome prediction. Nevertheless, there are only a few studies on EEG alterations in the earliest phase of ischemic stroke, <4.5h from symptom onset [13, 14]. EEG alterations were found to be strongly related to neurological deficit in this hyper-acute phase [14]. However, it would be of great research and clinical interest to assess also the relation between EEG parameters and the hypoperfused volume measured by CTP, as possible real-time surrogate parameters for extent of brain ischemia.

This preliminary study aimed at investigating the relation between stroke-related EEG changes, measured on bedside with wireless EEG device, and the extent of hypoperfused volume assessed on CTP during the hyper-acute phase.

2. Materials and methods

2.1. Study population

Twelve consecutive acute ischemic stroke patients (4M/8F, age median=79.5 (range 62-89) years), admitted to the Stroke Unit of the Trieste University Hospital (Trieste, Italy), who underwent CTP imaging and EEG acquisition at the bedside within 4.5 hours from stroke onset were included in this preliminary study. Due to lower sensibility of CTP posterior circulation stroke patients were excluded. Previous stroke, hematic effusion, history of epileptic seizure and use of medications, such as: neuroleptic or benzodiazepines, were also exclusion criteria because of their effect on EEG.

All patients underwent standard neurological assessment at admission comprising National Institutes of Health Stroke Scale (NIHSS) examination and a multimodal CT imaging protocol, including cerebral non-contrast CT (NCCT), CT angiography (CTA) and CT Perfusion (CTP). In the timespan between CTP and the beginning of reperfusion treatment, if the conditions were suitable in the emergency setting, EEG was acquired with a prewired headcap and wireless device. After this assessment, eligible patients underwent thrombolysis and/or thrombectomy reperfusion treatment. The correlation between total hypoperfused estimated by CTP processing and calculated EEG spectral parameters were investigated.

The research was conducted according to the ethical principles of the Declaration of Helsinki. All participants provided their informed consent. This study was approved by the Regional Ethical Committee (Comitato Etico Unico Regionale—CEUR) of Friuli Venezia Giulia, Italy with approval number 115/2018.

2.2. EEG acquisition and processing

EEG was acquired at bedside within 4.5 h from stroke symptom onset by 19 channel 10–20 Ag/AgCl electrodes wireless headset and Be Plus LTM amplifier @64 channels Wi-Fi (EBNeuro, Florence, Italy). All electrode impedances were kept below 5 kΩ and sampling rate was set to 128 Hz. The off-line analysis were performed using scripts developed in MATLAB (MathWorks Inc., Natick, MA). The signals were digitally filtered with the 0.5–40 Hz 2nd order Butterworth bandpass filter and the first 60 s of the artifact free EEG were analysed. Power spectral density (PSD) was estimated for each channel using Welch's periodogram [18], averaged on 11 tracts of 10 s each, windowed with a Hann window, with 50% overlap. The relative power for each of spectral bands (delta: 1–4Hz; theta: 4–8Hz; alpha: 8–13Hz; beta: 13–30Hz) was calculated for each channel. The relative powers were obtained by normalizing with a total power across the 1–30 Hz range. In addition, (delta+theta)/(alpha+beta) ratio DTABR and (delta/alpha ratio) DAR were computed. Relative power for each band, DAR and DTABR parameters were averaged over all nineteen scalp electrodes.

2.3. CTP acquisition and processing

All CTP scans were acquired on a 256-slice Philips Brilliance iCT scanner (Philips Healthcare, Best, The Netherlands) at 80 kVp and 150–200 mAs. At initiation of scanning, 75 ml of contrast medium was injected intravenously at a rate of 4 ml/s, followed by a 40 ml of saline bolus. The three-dimensional axial acquisitions on a whole brain volume with a reconstruction of the slices set to 5 mm were performed. The acquisitions were carried out every 4 s, resulting in a total scanning time of 60 s. CTP source image processing was performed by Extended Brilliance Workstation v 4.5 (Philips Medical Systems, Best, Netherlands) and in-house developed in Matlab (MathWorks Inc., Natick, MA), as described in our previous studies [3, 4]. CTP analysis is summarized in Figure 1. The perfusion maps mean transit time (MTT), cerebral blood volume (CBV) and cerebral blood flow (CBF) were calculated from source CTP. Gaussian curve fitting by least mean squares method was applied to obtain mathematical descriptions of the time-density curves for each voxel. An arterial input function (AIF) and venous output are selected and subsequently a closed-form deconvolution was applied to calculate a MTT map. CBV map was estimated from the area under the time attenuation curve and finally CBF map was calculated as a ratio between CBV and MTT. Core and penumbra areas were identified by application of specific thresholds [19], i.e. MTT voxels >145% of the contralateral healthy area and CBV<2.0 mL/100 g, and MTT voxels > 145% of the contralateral healthy area and CBV>2.0 mL/100 g, respectively. Total ischemic volume (core + penumbra) excluding artefacts was calculated by integration of identified ischemic core and penumbra voxels as previously described [3].

2.4. Statistical analyses

The degree of correlation between total hypoperfused volume and the EEG parameters was investigated by the Spearman correlation. The Kruskal-Wallis test with Tukey's post hoc test was used to determine the differences among frequency bands [20, 21]. A p-values below 0.05 were considered statistically significant.

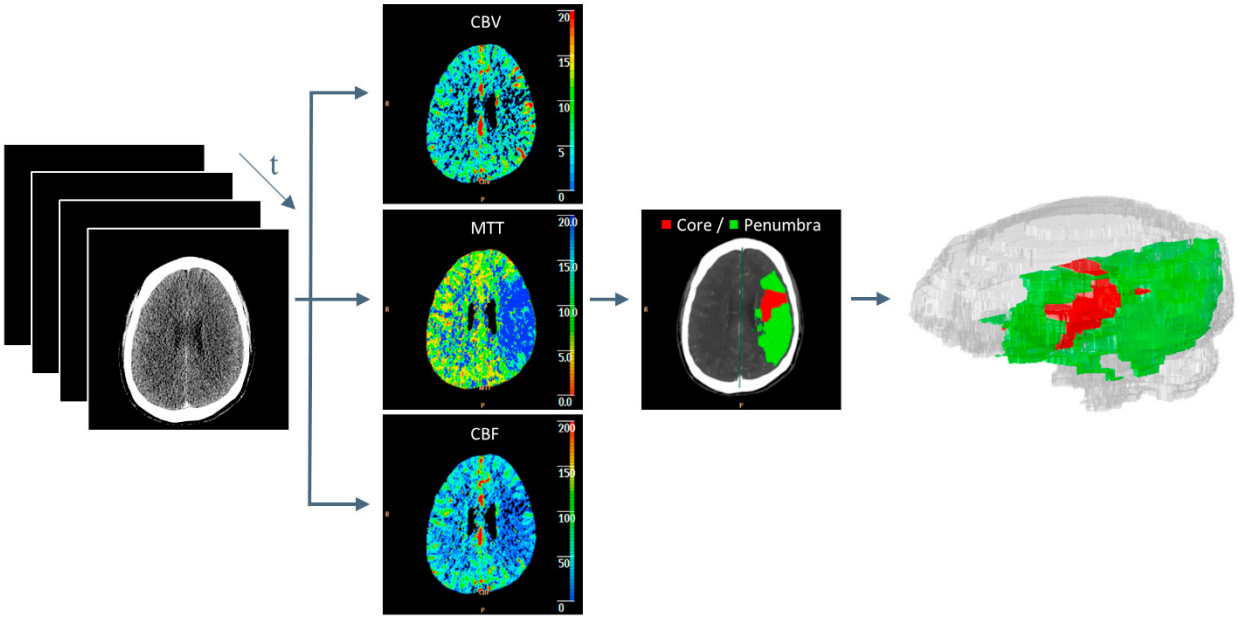

Fig. 1. CTP analysis on a single participant. From left to right: Source CTP data; CBV, MTT and CBF calculated maps, from top to bottom, respectively; core(red)/penumbra (green) map; 3D representation of total hypoperfused volume (core+penumbra).

3. Results

Table 1 summarizes radiological, clinical and demographic data of our study sample. Regarding the stroke severity, the median NIHSS at admission was 8.5 (range 3–23) and median ASPECTS of 9 (range 6–10) was observed on NCCT. Median time between stroke symptoms onset and performed EEG recording was 192 min (range 90–245 min). Relative power of theta, delta, alpha and beta EEG bands, DAR and DTABR calculated ratios, as well as their correlation with total ischemic volume are reported in Table 2.

Table 1. Patients' demographic, clinical and neuroimaging data.

Sex (F/M)	8/4
Age median (range)	79.5 (62-89) years
Lesion side (L/R)	5/7
ASPECTS median (range)	9 (6-10)
NIHSS median (range)	8.5 (3-23)
Total ischemic volume median (range)	50.9 (2.0-219.2) ml

The median relative delta, theta, alpha and beta power were 0.43 (range 0.33–0.67), 0.20 (range 0.10–0.35), 0.14 (range 0.06–0.38) and 0.13 (range 0.06– 0.22), respectively. Relative theta band resulted significantly higher comparted to other bands ($p<0.006$). The median DAR value was 3.38 (range 1.2–7.35) and median and DTABR values 2.81 (range 1.1–4.66), respectively. The calculated total ischemic volume was median=50.9 (range 1-219.2) ml.

Total ischemic volume correlated significantly with DAR ($\rho = 0.72$; $p< 0.010$), DTBAR ($\rho = 0.68$; $p=0.018$), as well as with relative delta ($\rho = 0.61$, $p<0.041$). In addition, significant negative correlation was found between hypoperfused volume and relative alpha power ($\rho = -0.77$; $p=0.003$).

Table 2. Correlation between EEG parameters and CTP total hypoperfused volume.

EEG spectral parameters	Median (range)	Spearman's ρ (p-value)
Relative δ	0.43 (0.33-0.67)	0.61 ($p < 0.041$)
Relative θ	0.20 (0.10-0.35)	NS
Relative α	0.14 (0.06-0.38)	-0.77 ($p = 0.003$)
Relative β	0.13 (0.06-0.22)	NS
DAR	3.38 (1.2-7.35)	0.72 ($p < 0.010$)
DTABR	2.81 (1.1-4.66)	0.68 ($p = 0.018$)

Note: NS – not significant.

4. Discussion

The evolution from ischemia to infarction in the acute phase of ischemic stroke is a dynamic rapidly developing process with irreversible cellular death occurring in hypoperfused brain tissue within a few minutes to a few hours [17]. Neurophysiological changes in the brain tissue during hypoperfusion, as expression of neurovascular coupling, are related to EEG alterations.

The main finding of this study is identification of a significant correlation between stroke-related EEG alterations and the total hypoperfused volume measured by CTP, during the hyperacute phase of ischemic stroke (<4.5h from symptom onset). In particular, DAR, DTBAR and relative delta power correlated directly, while alpha correlated inversely with CTP hypoperfused volume.

Portable wireless device allowed our study to adopt early EEG recording without delaying the treatment and compromising the patient management. The wireless EEG device acquired analog EEG electrical signals at a point close to the electrodes and subsequently transmitted EEG digital signals via Wi-Fi protocol to a base station. This allowed to minimize movement of electrode wires, a major source of electromagnetic interference [22] and electrode displacement that dramatically degrades EEG signal quality. Our study also showed that adequate acceptable quality of EEG data can be obtained in such adverse recording conditions as stroke-emergency setting. The state-of-the-art portable technologies may overcome most of EEG application inhibiting factors occurring in emergency settings such as stroke units [23, 24].

Different studies were focused on the comparison of EEG oscillatory activity and the ischemic area identified by neuroimaging. The combination of electrical oscillatory activity and neuroimaging has successfully demonstrated that the foci of abnormal EEG delta waves correlate well with areas of cerebral infarct identified by NCCT, CTP, PET and MRI [12, 13, 15, 25, 26]. A comparison between NCCT, performed 4 days after stroke's onset, and EEG, recorded within 24 h of onset, showed a relation between the site of increase of delta power and anatomical position of parenchymal damage [12]. Nevertheless, NCCT does not allow the identification of morphologic changes of the brain in the hyperacute of ischemic stroke [26]. For this reason, there is great research interest in the joint analysis of the neurophysiological and hemodynamic activity in the earliest phase of ischemic stroke. EEG recording within diffusion-weighted imaging (DWI) - perfusion-weighted imaging (PWI) MRI sequences allows direct correlation of stroke-induced EEG abnormalities with functional MRI changes [27]. A modest correlation between alteration of delta activity recorded by EEG and 15- hours MRI-DWI was also reported [16]. A recent study reported agreement between slow rhythms hemispheric prevalence on EEG maps and cerebral hypoperfusion area identified using CTP [13]. Nevertheless, no previous study investigated the relation between hypoperfused volume assessed on CTP maps and EEG stroke-related changes in the earliest phase of ischemic stroke.

EEG alterations, especially in terms of DAR, DTBAR and relative alpha are related to neurological deficit at admission [14] and are correlated in acute phase and in sub- acute phase are related to functional outcome [15, 16]. EEG changes observed in our study are consistent with previous studies.

In conclusion, we preliminarily assessed the relation between EEG alterations in earliest phase of ischemic stroke and hypoperfused volume assessed by CTP. These results highlight the value of EEG as a possible complementary tool in the evaluation of stroke severity and its potential role in acute stroke patient longitudinal monitoring in hyper-acute phase.

Acknowledgements

The work is partially supported by Master's in Clinical Engineering - University of Trieste.

References

[1] Gorelick, P. B. (2019) "The global burden of stroke: persistent and disabling." *The Lancet Neurology* **18** (**5**): 417-418.

[2] Vilela, P., and Rowley, H. A. (2017) "Brain ischemia: CT and MRI techniques in acute ischemic stroke." *Eur J Radiol* **96**: 162–172.

[3] Furlanis, G., Ajčević, M., Stragapede, L., et al. (2018) "Ischemic Volume and Neurological Deficit: Correlation of Computed Tomography Perfusion with the National Institutes of Health Stroke Scale Score in Acute Ischemic Stroke." *J Stroke Cerebrovasc Dis* **27**: 2200–2207. doi: https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.04.003

[4] Manganotti, P., Furlanis, G., Ajčević, M., et al. (2019) "CT perfusion and EEG patterns in patients with acute isolated aphasia in seizure-related stroke mimics." *Seizure - Eur J Epilepsy* **71**: 110–115. doi: https://doi.org/10.1016/j.seizure.2019.07.005

[5] Furlanis, G., Ajčević, M., Buoite Stella, A., et al. (2020) "Wake-up stroke: thrombolysis reduces ischemic lesion volume and neurological deficit." *Journal of neurology* **267**: 666–673. doi: https://doi.org/10.1007/s00415-019-09603-7

[6] Granato, A., D'Acunto, L., Ajčević, M., et al. (2020) "A novel Computed Tomography Perfusion-based quantitative tool for evaluation of perfusional abnormalities in migrainous aura stroke mimic." *Neurol Sci*. doi: https://doi.org/10.1007/s10072-020-04476-5 .

[7] Peisker, T., Koznar, B., Stetkarova, I., et al. (2017) "Acute stroke therapy: a review." *Trends Cardiovasc Med* **27**: 59–66.

[8] Gonzalez, R. G. (2006) "Imaging-guided acute ischemic stroke therapy: from "time is brain" to "physiology is brain"." *AJNR Am J Neuroradiol* **27** (**4**): 728–735.

[9] Ajčević, M., Furlanis, G., Buoite Stella, A., et al. (2020) "CTP based model predicts outcome in rTPA treated wake-up stroke patients." *Physiol Meas*. doi: https://doi.org/10.1088/1361-6579/ab9c70

[10] Parsons, M. W. (2008) "Perfusion CT: is it clinically useful?." *Int J Stroke* **3** (**1**): 41–50.

[11] Jordan, K. J. (2004) "Emergency EEG and continuous EEG monitoring in acute ischemic stroke." *J Clin Neurophysiol* **21**: 341–352.

[12] Murri, L., Gori, S., Massetani, R., et al. (1998) "Evaluation of acute ischemic stroke using quantitative EEG: a comparison with conventional EEG and CT scan." *Neurophysiol Clin* **28**: 249–57.

[13] Stragapede, L., Furlanis, G., Ajčević, M., et al. (2019) "Brain oscillatory activity and CT perfusion in hyper-acute ischemic stroke." *Journal of Clinical Neuroscience* **69**: 184-189. doi: https://doi.org/10.1016/j.jocn.2019.07.068

[14] Ajčević, M., Furlanis, G., Stragapede, L., et al. (2020) "Brain Oscillatory Activity and Neurological Deficit in Hyper-acute Ischemic Stroke: Correlation of EEG Changes with NIHSS." In: Proc Mediterranean Conference on Medical and Biological Engineering and Computing, Coimbra, 2019, *IFMBE Proceedings* **76**: 133-141. doi: https://doi.org/10.1007/978-3-030-31635-8_16

[15] Finnigan, S. P., Rose, S. E., Walsh, M., et al. (2004) "Correlation of quantitative EEG in acute ischemic stroke with 30-day NIHSS score. Comparison with diffusion and perfusion MRI." *Stroke* **35**: 899–903.

[16] Finnigan, S. P., Rose, S. E., Walsh, M., et al. (2007) "Quantitative EEG indices of sub-acute ischaemic stroke correlate with clinical outcomes." *Clinical Neurophysiology* **118** (**11**): 2525-2532.

[17] Sheorajpanday, R. V., Nagels, G., Weeren, A. J., et al. (2011) "Quantitative EEG in ischemic stroke: correlation with functional status after 6 months." *Clinical neurophysiology* **122** (**5**): 874-883.

[18] Welch, P. (1967) "The use of fast fourier transform for the estimation of power spectra: a method based on time averaging over short, modified periodograms." *IEEE Trans Audio Electroacoust* **15** (**2**): 70–73.

[19] Wintermark, M., Flanders, A. E., Velthuis, B., et al. (2006) "Perfusion-CT assessment of infarct core and penumbra." *Stroke* **37** (**4**): 979–85.

[20] Kruskal, W. H., and Wallis, W. A. (1952) "Use of ranks in one-criterion variance analysis," *Journal of the American Statistical Association* **47**: 583–621.

[21] Hochberg, Y., and Tamhane, A. C. (1987) "Multiple Comparison Procedures." Hoboken, NJ: John Wiley & Sons.

[22] Usakli, A. B. (2010) "Improvement of EEG signal acquisition: an electrical aspect for state of the art of front end." *Comput Intell Neurosci* **2010**: 630649. doi: https://doi.org/10.1155/2010/630649

[23] Debener, S., Minow, F., Emkes, R., et al. (2012) "How about taking a low-cost, small, and wireless EEG for a walk?." *Psychophysiology* **49**: 1617–1621. doi: https://doi.org/10.1111/j.1469-8986.2012.01471.x

[24] David Hairston, W., Whitaker, K. W., Ries, A. J., et al. (2014) "Usability of four commercially-oriented EEG systems." *J Neural Eng* **11**: 46018. doi: https://doi.org/10.1088/1741-2560/11/4/046018

[25] Nagata, K., Tagawa, K., Hiroi, S., et al. (1989) "Electroencephalographic correlates of blood flow and oxygen metabolism provided by positron emission tomography in patients with cerebral infarction." *Electroencephalogr Clin Neurophysiol* **72** (**1**): 16–30.

[26] Chalela, J.A., Kidwell, C.S., Nentwich, L.M., et al. (2007) "Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison." *The Lancet* **369** (**9558**): 293–298.

[27] Moyanova, S.G., and Dijkhuizen, R. M. (2014) "Present status and future challenges of electroencephalography- and magnetic resonance imaging-based monitoring in preclinical models of focal cerebral ischemia." *Brain Res Bull* **102**: 22–36.