

Glaucoma has a Cerebral Component: a TD-fNIRS Study

R. Re^{*1,2}, D. Messenio³, G. Marano⁴, L. Spinelli², I. Pirovano¹, D. Contini¹, R. Colombo³, P. Boracchi⁴,
E. Biganzoli^{4,5}, R. Cubeddu¹, and A. Torricelli^{1,2}

¹Dipartimento di Fisica, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milan, Italy; ²Istituto di Fotonica e Nanotecnologie, Consiglio Nazionale delle Ricerche, Piazza Leonardo da Vinci 32, 20133 Milan, Italy; ³Eye Clinic, Department of Clinical Sciences, ASST Sacco Hospital, University of Milan, Milan, Italy; ⁴Laboratorio di Statistica Medica, Biometria ed Epidemiologia "G.A. Maccacaro", Dipartimento di Scienze Cliniche e di Comunità, Università degli Studi di Milano, Via Vanzetti 5, Milan, Italy; ⁵Unità di Statistica Medica, Biometria e Bioinformatica, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Via Vanzetti 5, Milan, Italy.
rebecca.re@polimi.it

Abstract: A study on 118 subjects, performed with TD-fNIRS, demonstrated that the glaucoma has a cerebral component. The fNIRS parameters that best represent this finding are the OHB and HHB amplitudes, as revealed by PCA. © 2020 The Author(s)

1. Introduction

Glaucoma is a neuropathy of the eye characterized by a progressive loss of the vision capacity. In human studies degenerative changes in the brain involving the visual cortex have been recently found with magnetic resonance imaging [1]. The aim of this work was to assess the relationships between measurements on the visual cortex, obtained with a non-invasive optical technique, and results of morphological evaluation of eyes in order to understand more clearly if there is a cerebral involvement in patient with glaucoma respect to healthy subjects. The optical technique employed is time-domain functional near infrared spectroscopy (TD-fNIRS), which allows to monitor the brain hemodynamic function, enhancing the brain cortex contribution in the detected signal, with respect to more superficial contributions due to the scalp, skull and skin [2].

2. Material and methods: subjects, instruments and data analysis

We enrolled 118 subjects: 4 were not eligible for clinical reasons and did not took part to the acquisition session. The study received the approval of the Ethical Committee of Sacco Hospital and was conducted in compliance with the Declaration of Helsinki. A set of a standard clinical exams have been carried out in order to classify the patient eyes status. These exams are: transient Pattern Electroretinogram (PERG); Visual Evoked Potentials (VEPs); visual acuity; Goldman applanation tonometry; computerized visual field (G2 program, Octopus perimeter), OCT (RNFL and macular ganglion cell thickness). According to the results of these standard tests, the subjects were classified as healthy (NORM); ocular hypertension patients (HYPER): subjects with intraocular pressure (IOP) >21 mmHg in the absence of clinical signs of glaucoma and glaucoma patients with a structural damage at the optic nerve head and visual field loss. The latter was split in Open Angle Glaucoma (OAG, IOP>21 mmHg) and Normal Tension Glaucoma (NTG, IOP <21 mmHg) before lowering IOP therapy. Each subject sat in front of a monitor at a distance of 130 cm and had to fix its center with one eye at a time. The visual stimulus employed was a pattern reversal checkerboard (check size 1.13 cm side, reversal frequency 10 Hz). After 30 s of initial baseline, 5 repeated cycles (10 s rest, 10 s visual stimulus, 10 s recovery) were presented to the subject. The rest and recovery screens were grey, with an equivalent luminance to the checkerboard. The injection optical fiber was placed in the OZ position, the detection ones in the O1 and O2 respectively, accordingly to the standard 10-10 system of EEG electrode positioning, resulting in two measurement points, one per hemisphere. The TD-fNIRS medical device is described in the work by Re *et al.* [3]. To estimate the baseline optical properties (absorption and reduced scattering coefficients), the TD-fNIRS reflectance curves at both wavelengths (687 nm and 826 nm) were fitted with the solution of the diffusion equation for a semi-infinite homogeneous medium, after convolving with the instrument response function. We checked the measurement quality in terms of detected photons number (>150 kcounts in the baseline) and fitting parameter ($\chi^2 \leq 2$). Variations of the cortical oxy- (OHB) and deoxy- (HHB) haemoglobin concentration were obtained with a method based on the computation of the mean time pathlengths travelled by the photon in a 2-layer medium [4]. We then determined the maximum (minimum) amplitude (A) for the OHB (HHB) for each repeated stimulation and delay (τ) respect to the stimulus onset, by fitting the OHB and HHB time courses with a canonical hemodynamic response function [5]. For TD-fNIRS parameters, a descriptive analysis was performed as a preliminary investigation of the sources of variability related to the experimental factors (inter and intra subjects' variability). Boxplots and trellis plots were then used. In order to evaluate the relationships among eye morphology and TD-fNIRS parameters, the multivariate correlation structure by Principal Component Analysis (PCA) method

was performed. The relationships between couples of variables, highlighted in maps, were synthesized using Pearson's correlation coefficient (r). TD-fNIRS parameters were passively projected onto the PCA maps.

3. Results

After the acquisitions we should eliminate other 8 subjects: 1 subject was not collaborative, 2 had a wrong optodes positioning and 3 didn't pass the TD-fNIRS quality check. Furthermore, in 2 subjects, with head diameter >61 cm, we could not place the EEG cap in the right position and we had to discard them. The final number of subjects included in the statistical analysis was 106. For each subject, we considered the single eye and hemisphere. We had a total of 212 eyes and 424 hemispheres. Performing the signal quality check on the single acquisition channel, we eliminated some channels more, having as final results: 209 eyes and 416 hemispheres. On the basis of the standard clinical exams, the subjects and eyes were classified as: 31 NORM (61 eyes), 20 HYPER (40 eyes), 24 NTG (48 eyes), 19 OAG (36 eyes), 8 with 1 eye NORM and 1 NTG, 4 with 1 eye NORM and 1 OAG. In the descriptive analysis, subjects showed regular patterns in term of A and τ values for both the OHB and HHB. For what concerns the behavior of A and τ versus the diagnosis, A data distributions were lower (higher) in NORM eyes respect to the glaucomatous eyes for HHB (OHB) measurements, while no significant difference emerged for the distributions of τ data. From the PCA analysis of the traditional diagnostic parameters (Fig. 1(a); explained variability: 51.6% for the first PC. 12.1% for the second PC), we found a positive correlation ($r=0.78$) between the mean defect (MD, diffuse damage index) and corrected loss variance (CLV, localized damage index), among OCT variables ($r: 0.32$ to 0.96), between PEV15 and PEV30 ($r=0.87$), PERG15 and PERG30 ($r=0.54$); while there is a negative correlation among MD, CLV and OCT parameters ($r: -0.73$ to -0.43). Overall, NORM and HYPER eyes, differ from NTG and OAG in terms of MD, CLV and OCT parameters. In Fig. 1(b) and (c), we show the passive projections of A for HHB and OHB respectively. The correlation with the active variables is low ($r: -0.22$ to 0.27), however an interesting pattern it was revealed: the HHB (OHB) vectors head towards the left (right), i.e. towards NTG and OAG (NORM and HYPER) eyes. This pattern suggests an association between eye pathological classification and OHB and HHB amplitudes. This is in agreement with a higher cerebral activation (increase in OHB and decrease in HHB) in the control group compared with the glaucomatous one. The fNIRS parameter τ for both HHB and OHB, show low correlation ($r: -0.28$ to 0.28) with the active variables and no specific pattern.

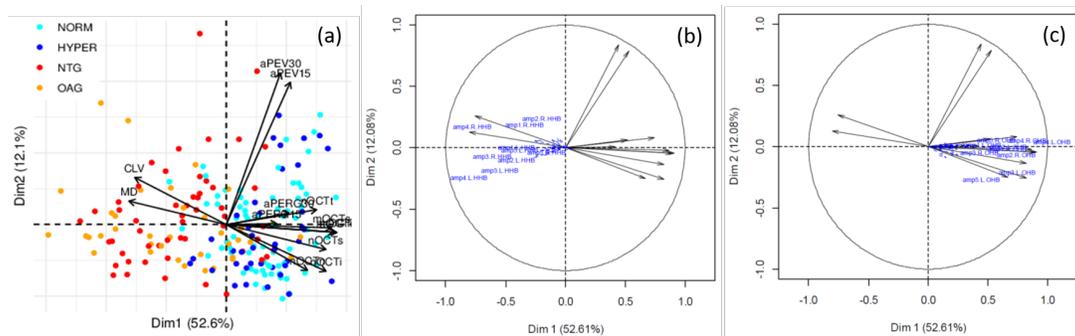


Fig. 1. PCA results: (a) traditional diagnosis parameters (b) HHB amplitude (c) OHB amplitude.

4. Conclusions

We realized a study on 118 subjects to understand if the glaucoma has a visual cortex component in terms of activation. We performed TD-fNIRS measurements on the visual cortex, together with the standard diagnostic exams. We noticed that the amplitude of the hemodynamic response shows a different pattern in the glaucomatous group with respect to the control one.

4. References

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