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TD-fNIRS for diagnosing glaucoma: a clinical pilot study

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ABSTRACT

Glaucoma is a multifactorial optic neuropathy characterized by progressive loss of retinal ganglion cells, changes in optic disk morphology and visual field defects; its pathophysiology is still unclear. Recently it was demonstrated that glaucoma can be associated with a degenerative effect at the level of the optic nerve and the primary visual cortex. Functional near infrared spectroscopy (fNIRS) is a non-invasive optical technique, which allows the brain hemodynamic monitoring. In particular, the Time Domain fNIRS (TD-fNIRS) allows to remove from the detected signal the contribution coming from the surface (scalp, skull and cerebral fluid) in order to obtain the brain hemodynamic activation. The aim of this preliminary study is to understand if in the glaucomatous patients, the visual cortex activation during a visual stimulus is different from the one of a control group. A total of 20 subjects took part to the study. We divided them into three groups: 7 controls, 5 ocular hypertension (HYPER), and 8 glaucoma. The hemodynamic time courses of oxy- (OHB) and deoxy- (HHB) hemoglobin were compared with a hemodynamic response function (HRF) with the adaptive HRF approach. Finally, an inference test was applied (t-student) to statistically determine the visual cortex activation (simultaneous increase in OHB and decrease in HHB). The p-value threshold was set at 0.05. The 86% of the controls and the 80% of the HYPER combinations are activated; while the 81% of the glaucoma ones are not, outlining a well-defined trend. Also the OHB and HHB show drastic differences between controls and patients.

Keywords: Time domain, near infrared spectroscopy, brain imaging, glaucoma, visual cortex, clinical spectroscopy

1. INTRODUCTION

Glaucoma is a multifactorial optic neuropathy characterized by progressive loss of retinal ganglion cells, changes in optic disk morphology and visual field defects. Glaucoma pathophysiology is still unclear. Intraocular pressure (IOP) is recognized as the most important risk factor for the development or progression of glaucomatous damage, even if pressure reduction does not necessarily slow or halt disease progression. The current diagnostic approach is based on morphologic and functional detection of retinal ganglion cell (RGC) losses by computerized optic nerve head analysis, for example, optical coherence tomography (OCT) as well as standard automated perimetry (SAP). Electrophysiological techniques as Visual Evoked Potentials (VEPs) and Pattern Electroretinogram (PERG) may help to identify subclinical functional deficits. Moreover, it was recently demonstrated that glaucoma can be associated with a degenerative effect at the level of the optic nerve and the primary visual cortex[1], in particular in the normal tension glaucoma (NTG). Functional near infrared spectroscopy (fNIRS) is a non-invasive optical technique, which allows the brain hemodynamic monitoring. In particular, the Time Domain fNIRS (TD-fNIRS) allows to remove from the detected signal the contribution coming from the surface (scalp, skull and cerebral fluid) in order to obtain the brain hemodynamic activation. The aim of this preliminary study is to understand if in the glaucomatous patients, the visual cortex activation during a visual stimulus is different from the one of a control group.

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2. MATERIAL AND METHODS

2.1 Subjects

A total of 20 subjects took part to the study. We divided them into three groups: 7 controls (2 male 5 female, 68.43±3.51 years), 5 ocular hypertension (HYPER, 2 male 3 female, 62.00±7.04 years) and 8 glaucoma (6 male 2 female, 66.25±13.76 years). All patients and control subjects underwent a full ophthalmologic examination, including visual acuity measurement, Goldmann applanation tonometry, computerized white-on-white G2 visual field testing (Octopus perimeter), spectral domain OCT (Heidelberg), PERG and VEPs. HYPER are subjects with IOP>21 mmHg in the absence of clinical signs of glaucoma; in glaucoma patients there is a typical appearance of structural damage at the optic nerve head and visual field loss, with IOP>21 mmHg (hypertension glaucoma) or <21 mmHg (NTG) before lowering IOP therapy. The study received approval of the Ethical Committee of Sacco Hospital and was conducted in compliance with the Declaration of Helsinki.

2.2 Experimental Protocol

A pattern reversal stimulation (30' checks, 1.13 cm side, 10 Hz reversal frequency) was used as visual stimulus. After 30 s of initial baseline, 5 repeated cycles (10 s rest, 10 s visual stimulus, 10 s recovery) were presented to the subject. During the rest and recovery period a grey screen, with equivalent luminance to the checkerboard, was set. The subjects, sat down at 130 cm from the screen, had to fix the centre of the screen with one eye at a time. According to the standard 10-10 system of EEG electrode positioning, the injection fiber was placed in the OZ position, one detection optode in the O1 position, and another detection channel in the O2 one, so that we had two measurement points, one per hemisphere. For each subject the Instrument Response Function (IRF) was acquired.

2.3 TD-fNIRS: device and data analysis

The TD-fNIRS clinical device employed, which is approved by the Italian Ministry of Health, it is described in the work by Re *et al*[2]. It employs two picosecond pulsed lasers (687 nm and 826 nm) and TCSPC boards for signal acquisition. Data at both wavelengths were fitted with the solution of the diffusion equation for a semi-infinite homogeneous medium, after convolving with the IRF[3]. We obtain the cortical concentration of the oxy- (OHB) and deoxy- (HHB) haemoglobin and their variations respect to the baselines with the "time gated" method described in Contini *et al*[4], which allows to remove from the detected signal the more superficial physiological contributions. The hemodynamic time courses were then compared with a hemodynamic response function (HRF) with the adaptive HRF approach[5]. Finally, an inference test was applied (t-student) to statistically determine the visual cortex activation (simultaneous increase in OHB and decrease in HHB). The p-value threshold was set at 0.05.

3. RESULTS AND DISCUSSION

In Figure 1, we show the typical behavior of the results for both the hemispheres, for a control subject (a) and glaucoma patient (b), for both the hemispheres, when they are looking at the screen with the right eye. With the thin lines we represented the hemodynamic changes respect to the baseline of the OHB (red) and HHB (blue) during the 5 repeated cycles (in gray the period when the checkerboard is shown). With the thicker lines we indicate the fit with the HRF. Above the figures the p-values for both the hemoglobin are reported. When one of them is higher than 0.05 we cannot declare an activation, indicated with red font. When both are lower than 0.05 there is an activation, indicated with black font. Almost all the controls show the qualitative behavior of Figure 1 and almost all the glaucoma patient had flat or just outlined curves; sometimes they also showed a de-activation. There was not a standard trend behavior for the HYPER group (not shown), their activation amplitude seems lower and not always well defined. In addition, in Table 1 a list of the activations for all the subjects (all the watching eyes and hemispheres) is reported. The 86% of the controls and the 80% of the HYPER combinations are activated; while the 81% of the glaucoma ones are not, outlining a well-defined trend.

4. CONCLUSION

To our knowledge this is the first study where the statistical activations of the visual cortex are studied with TD-fNIRS in glaucomatous patients. Since this pilot clinical study shows drastic differences between controls and patients, we will improve the number of subjects during next months (>30 per each group) in order to confirm TD-fNIRS as a tool for diagnosing glaucoma. We will also refine the data analysis models for TD-fNIRS, take different parameters into account

(i.e. amplitude and delay in activation) and perform comparison with the other classical examinations, which the subjects underwent.

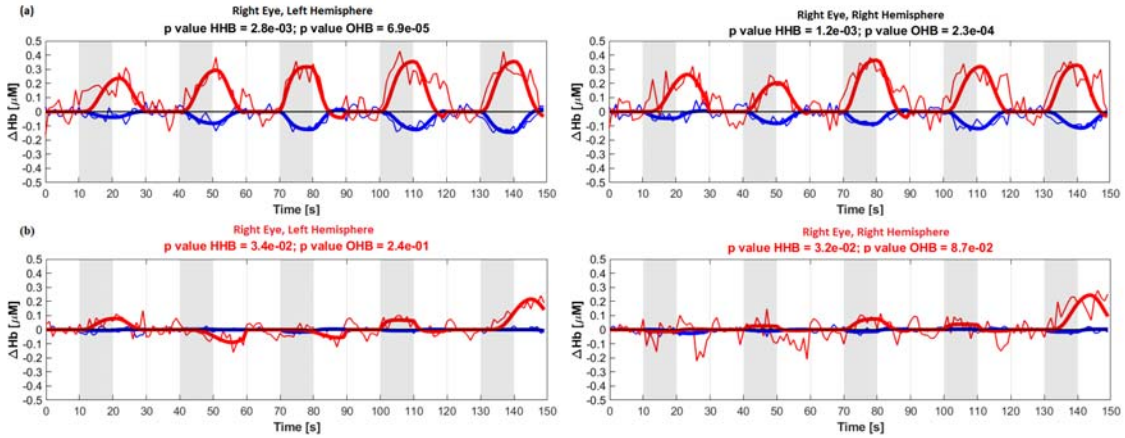

Figure 1. Time courses of OHB (red) and HHB (blue), thin lines. In grey the periods with the visual stimulus. The thick lines are the fit with the HRF. (a) Control subject. (b) Glaucoma patient.

Table 1. List of visual cortex activations for all the subjects based on p-value analysis. "YES": activated; "NO": not activated. "EYE": R=the subject is watching with the right eye; L=the subject is watching with the left eye. "Hemisphere": R=right; L= left.

CONTROL						GLAUCOMA					HYPER				
Eye	R	R	L	L		R	R	L	L			R	R	L	L
Hemisphere	L	R	L	R		L	R	L	R			L	R	L	R
C1	YES	YES	YES	YES	G1	NO	NO	NO	NO		H1	YES	YES	YES	YES
C2	YES	YES	YES	YES	G2	NO	NO	NO	NO		H2	YES	YES	YES	YES
C3	NO	NO	YES	NO	G3	YES	YES	NO	YES		H3	YES	NO	YES	NO
C4	YES	YES	YES	YES	G4	NO	NO	NO	NO		H4	YES	YES	YES	YES
C5	YES	YES	YES	YES	G5	NO	NO	NO	NO		H5	YES	NO	NO	YES
C6	YES	YES	YES	YES	G6	YES	NO	YES	NO						
C7	YES	YES	NO	YES	G7	NO	NO	NO	YES						
					G8	NO	NO	NO	NO						

REFERENCES

[1] Gupta, N., Ang, L. C., Noel de Tilly, L., Bidaisee, L. and Yucel, Y. H., "Human glaucoma and neuronal degeneration in intracranical optic nerve, lateral geniculate nucleus, and visual cortex," Br. J. Ophthalmol. 90(6), 674-678 (2006).

[2] Re, R., Contini, D., Turola, M., Spinelli, L., Zucchelli, L., Caffini, M., Cubeddu, R. and Torricelli, A., "Multi-channel medical device for time domain functional near infrared spectroscopy based on wavelength space multiplexing," Biomed. Opt. Express 4(10), 2231-2246 (2013).

[3] Contini, D., Martelli, F. and Zaccanti, G., " Photon migration through a turbid slab described by a model based on diffusion approximation. I. Theory, " Appl. Opt. 36(19), 4587–4599 (1997).

[4] Contini, D., Spinelli, L., Torricelli, A., Pifferi, A. and Cubeddu, R., "Novel method for depth-resolved brain functional imaging by time-domain NIRS," Proc. SPIE 6629, 7 (2007).

[5] Uga, U., Dan, I., Sano, T., Dan, H. and Watanabe, E., "Optimizing the general linear model for functional near-infrared spectroscopy: an adaptive hemodynamic response function approach," Neurophotonics 1(1), 015004-1 (2014).