3951 – A0237

Visually and Auditory Induced Event-Related Brain Dynamics in Glaucoma

Masaki Nakanishi[1,2]
Alberto Diniz-Filho[1]
Erwin R. Boer[1]
Ahmed Elhosseiny[1]
Tzyy-Ping Jung[2]
Felipe A. Medeiros[1]

[1] Visual Performance Laboratory, Department of Ophthalmology, University of California San Diego, La Jolla, CA, United States.
[2] Swartz Center for Computational Neuroscience, Institute for Neural Computation, University of California San Diego, La Jolla, CA, United States.

INTRODUCTION

- Glaucoma is a leading cause of irreversible visual impairment, which can significantly affect many activities of daily living.
- Performance-based assessment of visual impairment in glaucoma using driving simulation has been proposed to evaluate the effect of the disease on driving safety.[1,2]
- Although previous studies have shown significant differences in driving performance between glaucoma and healthy subjects, there is still a need to clarify the primary mechanisms responsible for degraded performance in glaucoma patients.
- A recent study has shown that glaucoma might compromise not only visual function but also auditory temporal processing.[3] Therefore, one might speculate whether deficits in auditory processing in patients with glaucoma could contribute to degraded performance during certain daily activities, such as driving.
- Event-related potentials (ERPs), which are time-locked electroencephalogram (EEG) patterns elicited by sensory events, have been used to investigate human brain function including visual and auditory processing.[4]
- Combining performance-based assessment and visual/auditory-induced ERPs could potentially provide meaningful information about the impact of glaucoma on brain function and task performance.

PURPOSE

- This study aimed to investigate biological EEG markers to evaluate perceptual states in glaucoma patients while performing activities of daily living, such as driving.

METHODS

Experiment 1

- 13 patients with glaucomatous visual filed loss and 13 control healthy subjects were enrolled in this experiment.
- A white square (5 cm each) was presented centrally on an LCD monitor and chirp signals with initial and target frequencies of 900 Hz and 1100 Hz, respectively, were presented centrally through an earphone (Figure 1).
- Each stimulus was presented for 100 ms, followed by a random interval of time selected within 1100 ms and 1400 ms before the next stimulus presentation.
- During the stimulus presentation, scalp EEG signals were recorded with a sampling rate of 500 Hz while performing the tasks with 19 active dry electrodes using wireless EEG Quick-20 Headset (Cognionics, Inc.) (Figure 2).

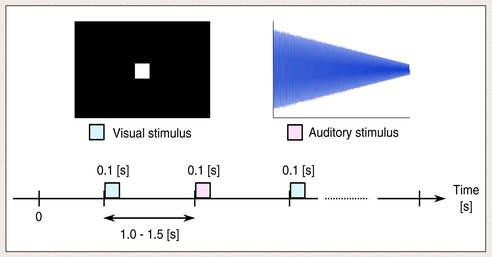

FIGURE 1. Experiment design to induce visual and auditory event-related potentials.

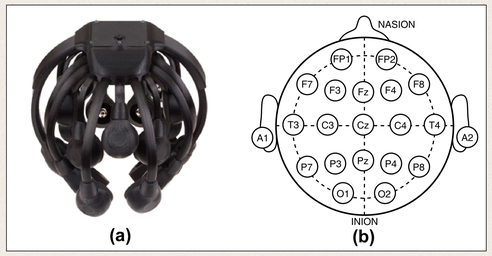

FIGURE 2. (a) Electroencephalograph (b) Electrode location following the international 10-20 system

Experiment 2

- 6 patients with glaucomatous visual filed loss and 6 control healthy subjects participated in this experiment.
- The primary task in the experiment was simulated driving in a curve negotiation task, in which the subjects were instructed to drive in the center lane on a winding 3-lane road at a constant speed of 55 MPH (Figure 3).
- A white square (5 cm each) was presented on an LCD either centrally or on the peripheral visual field while subjects were driving. Subjects were asked to respond to the stimuli by pressing a button on the steering with their thumb, which doesn't interfere the primary driving task.
- Driving performance was evaluated by inverse time to line crossing (InvTLC) which is defined as the time it would take the car to leave the lane if the current heading were maintained.
- EEG signals were also recorded while performing the driving task using the same device as the experiment 1.

FIGURE 3. A subject performing the driving tasks

REFERENCES

1. Medeiros FA, Weinreb RN, Boer ER, Rosen PN, Driving Simulation as a Performance-based Test of Visual Impairment in Glaucoma, *J Glaucoma*, 2012; 21(4): 221-227.
2. Tatham AJ, Boer ER, Gracitelli CPB, Rosen PN, Medeiros FA. Relationship between motor vehicle collisions and results of perimetry, useful field of view, and driving simulation in drivers with glaucoma, *Trans Vis Sci Tech*, 4(3): Article 5, 2015.
3. O'Hare F, Rance G, Crowston GC, McKendrick AM, Auditory and visual temporal processing disruption in open angle glaucoma, *Investigate Ophthalmology & Visual Science*, 2012, 53: 6512-6518.
4. Hillyard SA, Anrlo-Vento L, Event-related brain potentials in the study of visual selective attention, *Proc Natl Acad Sci USA*, 95: 781-787, 1998.
5. Sur S, Sihna VK, Event-related potential: A review, *Ind Psychiatry J*, 18(1):70-73, 2009.

Commercial Relationships: **Masaki Nakanishi**, None; **Alberto Diniz-Filho**, None; **Erwin R. Boer**, none; **Ahmed Elhosseiny**, None; **Tzyy-Ping Jung**, none; **Felipe A Medeiros**, Alcon Laboratories Inc (R), Alcon Laboratories, Inc (F), Allergan, Inc (F), Allergan, Inc (R), Allergan, Inc (C), Bausch & Lomb (F), Carl Zeiss Meditec, Inc (F), Carl Zeiss Meditec, Inc (R), Carl-Zeiss Meditec, Inc (C), Heidelberg Engineering, Inc (F), Merck, Inc. (F), National Eye Institute (F), Novartis (C), Reichert, Inc (R), Reichert, Inc (F), Sensimed (F), Topcon, Inc (F).

RESULTS

Experiment 1

- Mean age in the glaucoma and age matched control groups was 72.7 ± 10.5 years and 67.4 ± 9.0 years, respectively (P=0.178).
- Integrated binocular SAP mean sensitivity in glaucoma patients was significantly worse than in control subjects (22.83 ± 6.91 dB vs. 30.62 ± 1.59 dB, P<0.001).
- Empirical results showed that positive and negative potential changes related to visual and auditory perception, respectively, appeared at around 200 ms in the ERP images recorded from Cz channel, which is consistent to previous studies (Figure 5).[5]
- The averaged latency of visually induced ERPs in glaucoma patients was significantly larger than that in control subjects (241.08 ± 31.03 ms vs. 210.62 ± 16.03 ms, P=0.005).
- There was no significant difference in the latency of auditory induced ERPs between two groups (160.15 ± 19.02 ms vs. 156.52 ± 9.67 ms, P=0.273).

TABLE 1. Characteristics and metrics of subjects participated in the experiment 1.

	Glaucoma (n = 12)	Control (n = 12)	P-Value
Age, years	72.7 ± 10.5	67.4 ± 9.0	0.178
Gender, % female	15.38	46.14	0.200
SAP 24-2 MD of better eye, dB	-8.31 ± 7.07	-0.42 ± 1.00	<0.001
SAP 24-2 MD of worse eye, dB	-14.01 ± 9.22	-1.54 ± 1.85	<0.001
SAP 24-2 binocular MS, dB	22.83 ± 6.91	30.62 ± 1.59	<0.001
Visual response matrics			
ERP Amplitude, uV	0.54 ± 0.76	1.30 ± 1.96	0.462
ERP Latency, ms	241.08 ± 31.03	210.62 ± 16.03	0.005
Auditory response metrics			
ERP Amplitude, uV	-1.78 ± 1.25	-1.86 ± 1.24	0.761
ERP Latency, ms	160.15 ± 19.02	156.52 ± 9.67	0.273

SAP = standard automated perimetry; MD = mean deviation; dB = decibels; MS = mean sensitivity; ERP: event-related potentials

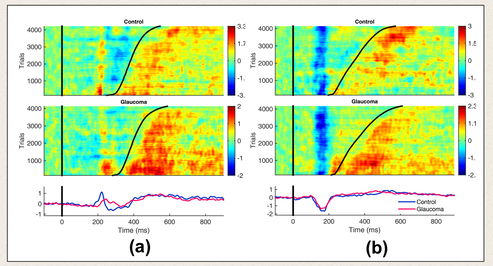

FIGURE 4. Event-related potentials induced by (a) visual and (b) auditory stimuli in control and glaucoma patients

Experiment 2

- Mean age in the glaucoma and control groups was 76.2 ± 5.7 years and 69.3 ± 8.9 years, respectively (P=0.144).
- Average SAP integrated binocular MS in glaucoma patients was significantly worse than in control subjects (27.92 ± 1.82 dB vs. 30.72 ± 1.55 dB, P=0.017).
- Driving performance on the central task (curve negotiation) was comparable between glaucoma and controls, as measured by InvTLC (0.162 ± 0.036 s^{-1} vs. 0.178 ± 0.035 s^{-1}, respectively; P=0.478).
- The latency of ERPs induced by central visual stimuli with low-contrast was negatively correlated with the InvTLC (R^2=19.2%, P<0.001).

TABLE 2. Characteristics and metrics of subjects participated in the experiment 2.

	Glaucoma (n = 6)	Control (n = 6)	P-Value
Age, years	76.2 ± 5.7	69.3 ± 8.9	0.144
Gender, % female	16.67	33.33	1.000
SAP 24-2 MD of better eye, dB	-2.01 ± 1.80	-0.25 ± 1.04	0.063
SAP 24-2 MD of worse eye, dB	-7.30 ± 2.80	-1.14 ± 1.71	<0.001
SAP 24-2 binocular MS, dB	27.92 ± 1.82	30.72 ± 1.55	0.017
Curve negotiation metrics			
InvTLC, s^{-1}	0.162 ± 0.036	0.178 ± 0.035	0.478

SAP = standard automated perimetry; MD = mean deviation; dB = decibels; MS = mean sensitivity; InvTLC: inverse time to line crossing

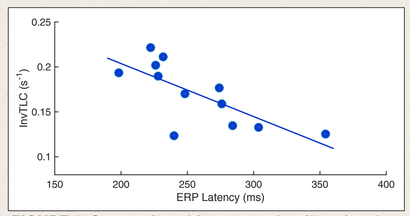

FIGURE 5. Scatterplot with a regression line showing the relationship between InvTLC and ERP latency

DISCUSSION

- The results showed a larger latency of visually induced ERP in glaucoma patients compared to control subjects, which is most likely caused by neural loss in glaucoma. There was no significant difference in the latency and amplitude of auditory induced ERPs between two groups, which suggests that glaucoma only affects visual processing and other stages of the response production are not affected in the disease.
- Although no significant differences in performance in the central driving task were seen between glaucoma and controls, glaucoma patients showed longer ERP latencies for detection of concomitant visual stimuli presented on the screen. This finding suggests that glaucoma patients could have longer delays in visual divided attention tasks while driving, which could significantly affect important activities, such as hazard detection.
- The current results agree with our previous investigations showing longer reaction times to divided attention tasks in glaucoma patients compared to controls. The use of ERP assessment in the current study adds significant information by clarifying that the longer reaction times are probably due to delayed visual processing rather than other mechanisms such as motor or auditory impairment.

CONCLUSION

- Our results suggest that glaucoma patients may take longer time to perceive visual stimuli than normal controls, which may negatively impact their daily activities.
- Latency of visually induced ERPs could be used to evaluate visual perceptual ability while performing daily activities in glaucoma patients.

Supported in part by NIH grants R01 EY021818, R21 EY025056, and core grant P30 EY022589, and fellowships from Brazilian National Council for Scientific and Technological Development (CNPq) 233829/2014-8.

mnakanishi@ucsd.edu