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Eyes as windows on brain pressure

Tarun Sinha [1]
Martin L. Lenhardt [1,2]

Abstract

The eyes are acoustically continuous with the brain and inner ear tissues as regards matched impedances, based on tissue densities; thus, vibration of one site will be reflected in all sites. As a result, the eye reflects the acoustic properties of the brain under pressure, which can be used as a metric of intracranial pressure as demonstrated in a brain/eye balloon model. Further, the model supports the observation that vibration delivered to the eye, if of sufficient intensity, can be perceived as sound, resulting in an eye audiogram similar to that obtained conventionally by bone conduction on the mastoid or forehead. The eye can therefore be considered an acoustical window to the brain and inner ear.

Keywords: eye sound conduction, intracranial pressure, intraocular pressure.

[1] Department of Biomedical Engineering, Virginia Commonwealth University.
[2] Ceres Biotechnology.
Correspondence: Martin L. Lenhardt, Au.D., Ph.D.
P.O. Box 980168 Virginia Commonwealth University
Richmond, VA 23298-0168.
lenhardt@vcu.edu

The old axiom that the eye is a window to the brain has not been found to be accurate as regards eye (intraocular) pressure reflecting brain (intracranial) pressure. Only one report has described an excellent correlation between the two pressures, suggesting a possible method of noninvasive intracranial pressure (ICP) measurement based on using intraocular pressure (IOP) alone[1]. However, that study result stands in stark contrast to others[2–7] that reported no correlation between ICP and IOP[7]. Perhaps sensing equipment variability was a factor in the positive report[8]. The recent retrospective study of Han et al[7]. is notable in finding no correlation of ICP with IOP in 55 patients in whom both measures were performed and concluded that the IOP is not a useful substitute for ICP. Sixty nine percent of these study patients suffered from pseudotumor cerebri, in which tinnitus is a common malady. The lack of pressure correlation is unfortunate in that a patented technology is available to measure the acoustic resonance of the eye, employing amplitude-modulated ultrasound to determine IOP[9]. Additionally, patent-protected technology exists to measure ICP using ultrasound applied to the skull and eye[10,11].

It is the purpose of this study to present data from an ICP-IOP balloon model that suggest the eye may indeed reflect the acoustical properties of elevated ICP without the need for pressure correlations. Supporting this model are reports that vibration applied to the eye is perceived as sound and the audiometric thresholds are similar to standard bone conduction and air conduction audiograms[12–15]. Thus, the eye may serve as an acoustic window to the brain and ear.

METHOD

A human skull/balloon model was used to simulate the fluid acoustics of the brain and eye. This model was used in previous studies with success, and details are presented there[16,17]. Briefly, a latex balloon was threaded through the orbit to simulate an eye, with the majority of the balloon body in the cranium (calvarium removed) simulating the brain; the balloon was then filled with water. A Radioear B-21 bone conduction transducer was affixed on the right supraorbital process and the accelerometer placed on the balloon "eye." The transducer input frequencies ranged from 250–1,000 Hz at 45–60 dB HL, generated by a Madsen Orbiter 922 audiometer (GN Otometrics A/S, Taastrup, Denmark) and calibrated on a Bruel and Kjaer, Nærum, Denmark (artificial mastoid (model 4930). A Measurement Specialties Incorporated (Hampton VA) model ACH-01 accelerometer recorded the vibration of the balloon eye. The accelerometer output was filtered, amplified, and fed into a Hewlett Packard dynamic signal analyzer Model 3561A (fast Fourier transform [FFT]) to quantify the vibration energy transmitted into the fluid-filled balloon "eye"; these values served as a baseline measurement for a nonpressurized balloon brain. The instrumentation setup is depicted in Figure 1. Markers were placed on the temporal bone, squamosal suture, and mastoid process, as well as on the occipital bone and frontal bone to maintain balloon position on repeated trials. Several audiometric frequencies (250–1,000 Hz) were applied to the bone transducer, and the accelerometer was placed at these locations to determine the resonance frequency amplitude. After several trials, the condition of 250 Hz at 45 dB was observed to produce the best resonance patterns and was selected to be the input frequency for determining changes when the brain was pressurized. Static pressure (~5 Newtons) was applied to the back end of the balloon, resting in the cranium, pressuring the "eye" by the balloon skin threaded through the back of the orbit (ocular nerve foramen).

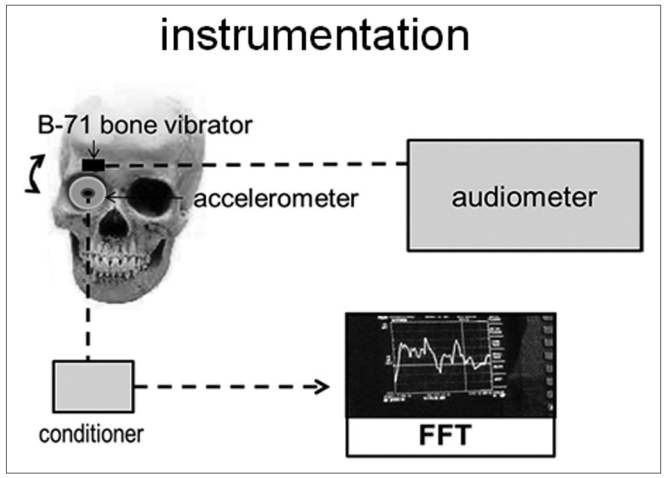

Figure 1. Instrumentation used in the study. Sounds were generated by an audiometer and delivered to either the skull or the eye (in the model) or, for the hearing tests, to the eye using a standard clinical bone conduction vibrator. Vibration of the balloon eye was recorded by a piezoelectric accelerometer, amplified and conditioned, and fed into a fast Fourier transform (FFT) for analysis.

After the skull model experiments, a second series on human subjects was studied under conditions of normal ambient brain pressure and elevated pressure using Valsalva maneuvers. The Valsalva maneuvers were performed in five young normal individuals (institutional review board–approved) using the aforementioned recording system and experimental protocol. Under normal conditions, the ICP varies between 1 and 10 mm Hg and, after Valsalva maneuvers, pressure can increase by an additional 5 to 10 mm Hg[18]. The effect on the acoustic transmission of pressuring the brain during Valsalva maneuvers was determined from the eye vibratory response.

The reverse brain–eye transmission, or the eye audiogram, was determined by delivering audio frequencies to the eye and obtaining standard audiometric

thresholds. The bone vibrator is placed on the eye and the accelerometer is affixed to the back of the vibrator to measure the output when mass loaded with the eye. The bone conduction transducer was firmly placed on the closed eyelids, carefully avoiding the bony rim of the orbit; the audible thresholds[19] for audiometric frequencies from 250 to 8000 Hz were obtained for each of the five subjects. Earplugs were inserted binaurally, and the pinnae were covered with Sennheiser sound-attenuating headphones (Sennheiser Electronic Corporation, Old Lyme, CT) to reduce the effects of ambient noise (attenuation of ~25 dBA) on thresholds.

RESULTS

When the forehead (supraorbital process) of the skull was driven by 500 Hz, the balloon eye responded with peak energy at the driving frequency (i.e., 500 Hz) accompanied by spectral energy spread above and below (25 dB down). When the brain was pressurized and the skull driven again at 500 Hz, the peak energy was also at 500 Hz but lower than the unpressurized condition by approximately 7 dBV (decibels re: 1 volt). Spectral spread was also present but damped (35 dB down), as depicted in Figure 2. Driving the skull at 250 Hz, the peak vibratory energy of the balloon eye was also at 250 Hz with spectral spread (above and below the driving frequency) of approximately 20 dB lower. However, when the brain was pressurized, the energy peak at 250 Hz was 12 dB lower than the unpressurized condition, with damped frequency spread (25 dB lower). An exception was observed at 300 Hz, which appeared to be a natural resonance of the balloon/brain model, as noted by the peak at the frequency when the skull is not excited by tonal stimulation. The undriven frequency response of this model was the baseline condition, as depicted in Figure 3. A similar resonance was found in direct eye resonance measurements[9].

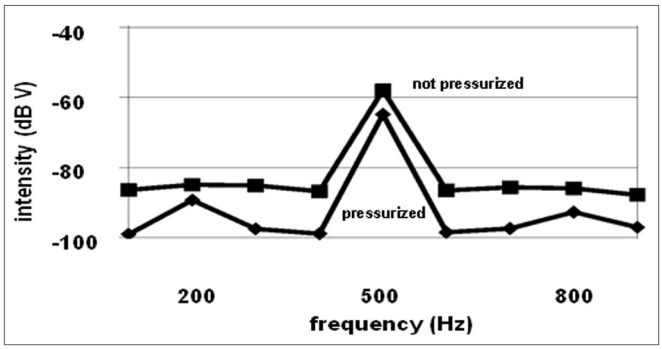

Figure 2. Vibratory response of the eye balloon as a function of frequency using a forced vibration of 500 Hz delivered by a vibrator on the skull. With pressurization of the balloon brain, the eye response is damped 7 dB (re: 1 volt).

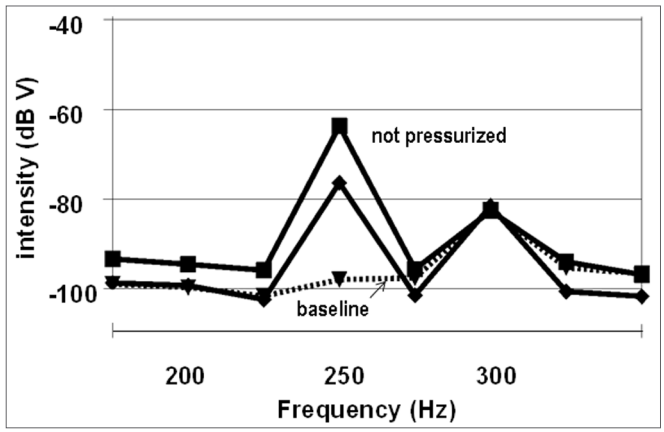

Figure 3. Vibratory response of the eye balloon with and without (baseline) forced vibration of the skull at 250 Hz. With pressurization, the response at the skull driving frequency (250 Hz) is damped by 12 dB (re: 1 volt).

When the skull was excited with low-frequency tones, the eye responded with sympathetic vibration. Pressurizing the brain resulted in a damped eye response—that is, reduced in amplitude at the driving frequency and reduced spectral spread.

Behavioral results from brain pressurization were obtained by recording the eye spectral response using broadband energy applied to the skin over the supraorbital process rather than tones, in an effort to reduce testing time and record the response over a broad range of frequencies. Pressurization of the brain and eye in vivo was accomplished by using a Valsalva maneuver, which increased the ICP. The Valsalva (pressurized brain) condition resulted in lowered vibratory response of the eye by 4–6 dB depending on frequency region. The main effect was at approximately 35 kHz, the presumed mechanical resonant frequency of the eye[20]. These data are presented in Figure 4. Frequency changes were noted for almost all frequency regions below the eye resonance (35 kHz). The in vivo human vibratory characteristics of a pressurized brain—that is, the eye's damped vibratory response—validates the skull/balloon model. The preferred eye recording site is the center, but the variation of the eye vibratory response was very small (<1 dB) over the surface. In contrast, slight movement of the accelerometer over the skin on the skull can result in large intensity differences (~5 dB)[21]. The variability over the skin of the skull limited clinical utility of this technique[10].

If the eye vibration reflects the skull/brain vibration, then eye vibration can also serve as an input to the brain if there is sufficient energy to stimulate the ear via the fluid pathway (cerebrospinal fluid). The concept of an eye audiogram is based on transmitting frequencies through the ocular fluid into the cerebrospinal fluid and determining subject threshold. The transducer was placed in the closed eyelid of the patient, and the intensity

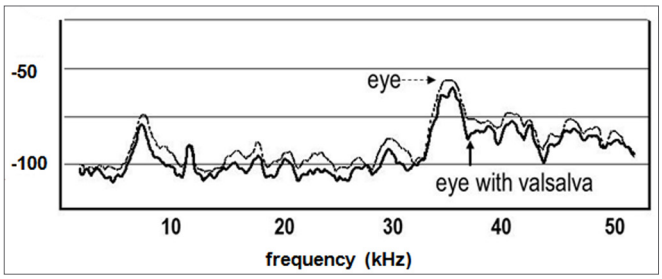

Figure 4. In one subject, vibration response of the eye induced by broadband noise delivered to the head. With pressurization (Valsalva maneuver), the vibratory response is damped over a wide frequency range by 4–6 dB (re: 1 volt). The natural resonance of the eye is approximately 35 kHz, with subharmonic peaks.

of the vibration varied in 5-dB steps to obtain threshold[19]. The results revealed responses in the normal range of bone conduction hearing, with the exception of the low frequencies owing to the ambient noise in the laboratory. Nonetheless, the average 250 Hz threshold was at 30 dB Hz and, for 500 Hz, was 9 dB higher. One thousand Hz was most efficiently transmitted through the eye with an average threshold of 0 dB HL. These thresholds (Fig. 5) indicate that the bone conduction transducer sent energy through the fluids in the brain to the ears, as had been previously suggested[12–14,20].

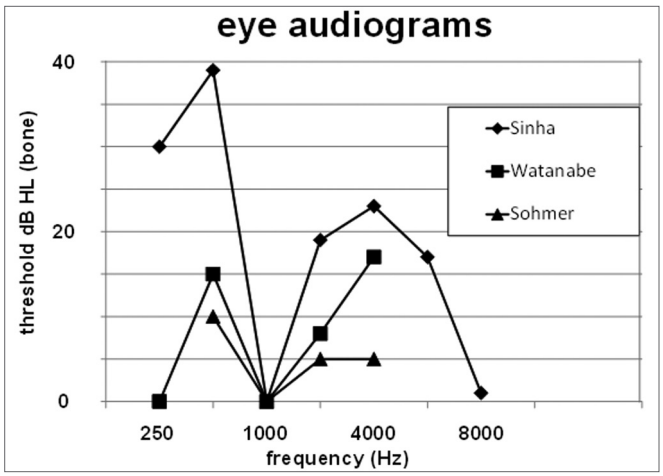

Figure 5. Eye audiograms as a function of bone conduction hearing level and frequency for five subjects (Sinha), contrasted to the data of Watanabe et al.[15] and Sohmer et al.[12–14] . Other than the ambient low-frequency noise masking in the Sinha data, the plots are in good agreement, with maximal sensitivity at 1,000 Hz. The eye is as sensitive as the skull, opening up the possibility of another method of stimulating the inner ear through a fluid conduction mechanism.

DISCUSSION

A clinical controversy exists regarding whether the pressure in the brain (ICP) and the pressure in the eye (IOP) correlate such that eye pressure alone could be used as a substitute for brain pressure. Such a noninvasive measure of ICP would be a valuable metric in diagnosis and treatment[22,23]. In a recent post hoc study on patients undergoing brain and eye pressure measurements, no correlation between the two was observed[7]. Though this was discouraging, it was not unexpected in that brain and eye the volumes differ and there is no direct connection; however, the optic nerve can act as an acoustic coupler between the brain and eye because all share the same acoustic impedance, as reflected in tissue densities (Table 1)[24]. Further, the brain can be considered a closed-boundary condition with few compliant windows, whereas the eye has only a semi-bone boundary. Thus, a positive pressure correlation is not necessary if, as in the present case, the acoustic response of the brain is reflected in the acoustic response of the eye, making a noninvasive measure possible. In the simplest explanation, the IOP damps eye vibration at the resonant frequency (and partial frequencies) and it is that reduced amplitude that may correlate and possibly predict ICP. The intensity reduction observed in our study was dependent on frequency and varied from 4 to 12 dB. Maximal frequency response was found at the fundamental resonance of the eye (32–36 kHz) during Valsalva maneuver. Most important, pressurized brain effects were observed at subharmonics as well. Sinha and Wray[9] measured the resonance of the eye at low frequencies and found biphasic peaks in the 280- to 310-Hz range, in agreement with the present findings (see Figures 2 and 3). The acoustic value was stable over the surface of the eye, in contrast to the well-reported variability on the skin over bone[21], which has limited the clinical usefulness of low-frequency intracranial acoustic approaches[10,11].

Table 1. Acoustic Impedance Similarity Based on Tissue Density for the Eye, Brain, and Ear.

Component	Density (kg/m^3)
Cornea	1,075
Humors	1.090
Optic nerve	1,093
Brain	1,093
Cerebrospinal fluid	1,004
Cochlear fluids	1,003

In 1930, Ranke[25] proposed that the cerebrospinal fluid connections, or any vascular connection to the cochlea, could act as an acoustic coupler. Tonndorf termed this coupler *the third window of Ranke*[26]. It has been demonstrated that direct audiofrequency vibration of the brain will couple to the ear and elicit evoked responses from the auditory nerve[12–14]. At frequencies near the eye resonance, air conduction sound will also couple to the ear via the eye[20], which may be the mechanism for

hearing damage for ultrasonic noise exposure in young workers[27–29], a matter that is addressed in current federal regulations[30]. These data all suggest that the brain can be a passive conductor of sound, even an amplifier near resonance[20,31], and at the same time a physiologic responder to the sound propagated through it. Thus, the channel from the eye through the brain to the ear has been clearly established.

CONCLUSIONS

The eye is a fluid globe that has an acoustic impedance match to the brain and ear. Pressurizing the brain in a balloon model resulted in detectable acoustic changes in the eye for a broad frequency range extending to the eye's ultrasonic resonance. Importantly, the eye's low-frequency response is stable and much less variable than that of the skin over the skull, making feasible the possibility of clinical use of this measurement tool. The use of audiofrequency rather than ultrasound is preferred in determining ICP noninvasively, because audio equipment is readily available and economical. Beyond feasibility is the necessity to obtain clinical data to explore efficacy. The eye audiogram was replicated and confirmed in the balloon model. The eye may have some advantages in delivering sound to the ear, but a prototype must be developed and tested for safety.

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REFERENCES

1. Sajjadi SA, Harirchian MH, Sheikhbahaei N, et al. Correlation of ICP and IOP. Ann Neurol. 2006;59:867–70.
2. Lehman RA, Krupin T, Podos SM. Experimental effect of intracranial hypertension upon intraocular pressure. J Neurosurg. 1972;36:60–6.
3. Smith RB, Aass AA, Nemoto EM. Intraocular and intracranial pressure during respiratory alkalosis and acidosis. Br J Anaesth. 1981;53:967–72.
4. Sheeran P, Bland JM, Hall GM. Intraocular pressure changes and alterations in intracranial pressure. Lancet. 2000;355:899.
5. Lashutka MK, Chandra A, Murray HN, et al. The relationship of intraocular pressure to intracranial pressure. Ann Emerg Med. 2004;43:585–91.
6. Czarnik T, Gawda R, Latka D, et al. Noninvasive measurement of intracranial pressure: is it possible? J Trauma. 2007:62:207–11.
7. Han Y, McCulley TJ, Horton JC. No correlation between intraocular pressure and intracranial pressure. Ann Neurol. 2008;8;64(2):221-4.
8. Wingert TA, Bassi CJ, McAlister WH, Galanis JC. Clinical evaluation of five portable tonometers. J Am Optom Assoc. 1995;66:670–4.
9. Sinha DN, Wray WO. Apparatus and method for non-contact, acoustic resonance determination of intraocular pressure. US Patent 5,375,595, 1994.
10. Lenhardt ML Non-invasive cerebral spinal fluid pressure monitor apparatus and method. US Patent Application 2003/0199784, 2003.
11. Lenhardt ML, Ward KW. Method and apparatus for monitoring intraocular and intracranial pressure. United States Patent Application 2007/0123796, 2007.
12. Freeman S, Sichel JY, Sohmer H. Bone conduction experiments in animals— evidence for a non-osseous mechanism. Hear Res. 2000;146:72–80.
13. Sohmer H, Freeman S, Geal-Dor M, et al. Bone conduction experiments in humans—a fluid pathway from bone to ear. Hear Res. 2000;146:81–8.
14. Sohmer H, Freeman S. Further evidence for a fluid pathway during bone conduction auditory stimulation. Hear Res. 2004;193:105–110.
15. Watanabe T, Bertoli S, Probst R Transmission pathways of vibratory stimulation as measured by subjective thresholds and distortion-product otoacoustic emissions. Ear Hear. 2008;29:667–73.
16. Dunlap S, Lenhardt ML, Clarke AM. High frequency skull vibratory pattern. Otolarynol Head Neck Surg. 1988;99:389–91.
17. Cai Z, Richards DG, Lenhardt M, Madsen AG. Response of human skull to bone-conducted sound in the audiometric-ultrasonic range. Int Tinnitus J. 2002;8(1):3–8.
18. Greenfield JC, Rembert JC, Tindall GT. Transient changes in cerebral vascular resistance during the Valsalva maneuver in man. Stroke. 1984;15:76–9.
19. Annex B of Methods for Manual Pure-Tone Threshold Audiometry (ANSI S3.21-2004).
20. Lenhardt, M.L. Eyes as fenestrations to the ears; a novel mechanism for high frequency hearing. Int Tinnitus J. 2007;13(1):3–10.
21. Richards DG, Lenhardt ML, Madsen AG. Non-Invasive Acoustic Measurement of Intracranial Pressure. In J Vossoughi (ed), Biomedical Engineering: Recent Developments. Washington, DC: Medical and Engineering Publishers, 2002:41–2.
22. Semmlow JL, Fisher R. A noninvasive approach to intracranial pressure monitoring. J Clin Eng. 1982;7:73–8.
23. Stevanovic M, Wodicka GR, Bourland JD, et al. The effect of elevated intracranial pressure on the vibrational response of the ovine head. Ann Biomed Eng. 1995;23:720–7.
24. Duck FA. Physical Properties of Tissues: A Comprehensive Reference Book. New York: Academic, 1990.
25. Ranke OF. Physiologie des Gehors. In OF Ranke, L Lullies, Gehor Stimme Sprache. Berlin: Springer, 1953:3–110.
26. Tonndorf J, Tabor JR. Closure of the cochlear windows Ann Otol Rhinol Laryngol. 1962;71:5029–35.
27. Parrack HO. Effects of airborne ultrasound on humans. Int Aud. 1966;5:294–308.
28. Grzesik J, Pluta E. High-frequency hearing risks of operators of industrial ultrasonic devices. Int Arch Occup Environ Health. 1983;53(1):77–8.
29. Grzesik J, Pluta E. Dynamics of high-frequency hearing loss of operators of industrial ultrasonic devices. Int Arch Occup Environ Health. 1986;57(2):137–42.
30. Occupational Safety Health Administration .Technical Manual, Section III, Chapter 5, subchapter V, Ultrasonics. Washington, DC: US Department of Labor, 2002.
31. Lenhardt ML. Ultrasonic hearing in humans: Applications for tinnitus treatment. Int Tinnitus J. 2003;9(2):69–75.