Title
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Journal
Aerospace Medicine and Human Performance (AMHP), 84(9)

ISSN
0095-6562

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Publication Date
2013-09-01

DOI
10.3357/asem.3575.2013

Peer reviewed

Published in final edited form as:
Aviat Space Environ Med. 2013 September ; 84(9): 995–1000.

Anterior-Posterior Transcranial Ultrasound to Measure Cranial Oscillations

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Abstract

Background: We aimed to provide information on whether or not the correlation between body tilt and the pulse amplitude of transcranial ultrasonic time-of-flight waveform can be observed in the anterior-posterior skull direction. Also, we asked the question whether or not the skull pulsation can be detected since the cranial bones involved are thicker.

Methods: The experimental model of body tilt that alters intracranial pressure by shifting body fluid headward was employed. Transcranial ultrasound waveforms were examined in 15 healthy volunteers positioned at five tilt angles of +30°, 0°, −30°, −60°, and −90° from the horizontal body position. A pulse-echo transducer was placed on the middle forehead and ultrasound waveforms were recorded. Synchronized variations in the ultrasonic time-of-flight with heartbeats were monitored using the pulsed phase locked loop technique for the output voltage of the ultrasound transducer. Simultaneous effects of body tilt on cardiovascular parameters were also evaluated.

Results: Pulse amplitudes of ultrasonic time-of-flight waveforms were found to vary with body tilt. Repeated-measures ANOVA and regression analysis showed a negative correlation between body tilt angle and pulse amplitude. The regression line has the equation: pulse amplitude = $(1.158 - 0.01023 \times \text{tilt angle}) \times 10^{-4}$ voltage. There was no such relationship between head-down body tilt and altered mean blood pressure or heart rate.

Conclusion: An increase in the pulse amplitude of the anterior-posterior transcranial ultrasonic time-of-flight waveform can be detected when the head-down body tilt angle increases.

Keywords

body tilt; cranial oscillation; human; ultrasound

RECENT OPHTHALMIC evaluations of seven astronauts after their 6-mo missions to the International Space Station revealed unexpected visual abnormalities (7). Among several

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possible explanations, elevated intracranial pressure (ICP) due to headward body fluid shift under microgravity (3) is considered the leading cause. Recent clinical observations also indicated that low ICP can play a role in primary open-angle glaucoma, a neurodegenerative disease of the optic nerve (1). Understanding biological impacts of ICP changes on the eye and vision requires ICP readings. While noninvasive determinations of accurate ICP have faced many technical challenges, surrogate measures are available (10). Among the surrogate methods for noninvasive ICP monitoring, ultrasonography offers the advantage of portability and versatility. These techniques include measurements of transcranial ultrasonic time-of-flight (14) and brain tissue resonance (9).

A working ICP range to study visual abnormalities in astronauts and glaucoma pathogenesis can be achieved using an experimental model of varying body tilt angles (4). After a +30° to −15° tilt with respect to the horizontal position (0°), the pulse amplitudes of transcranial ultrasonic time-of-flight waveforms synchronized with the heartbeats are enlarged and associated with an approximate 5-μm movement between the temporal bones (12). However, there is a concern that data obtained from this commonly used transverse orientation may be irrelevant to the intracranial force on the eye. Reports showed that shape of the intracranial ultrasound waveform between the frontal bone and the third ventricle (9) was different from the waveform between the temporal bones (14). The posture-related pulse amplitudes of transcranial ultrasound waveforms in the sagittal direction that are aligned with the retrolaminar subarachnoid space to the optic nerve head have not been studied. Since the anterior frontal bone and the posterior occipital bone are relatively thicker than the temporal bones, it was also unclear whether or not an anticipated smaller skull expansion due to head-down body tilt can be detected.

In the present study, we evaluated the transcranial ultrasound waveforms in the anterior-posterior skull direction using the experimental model of altering body tilt angles. The correlation between the body tilt angle and the pulse amplitude as well as the simultaneous effects on the cardiovascular parameters were studied in order to explore the usage of pulse amplitude of anterior-posterior transcranial ultrasound waveforms as a noninvasive surrogate measure of intracranial force on the eye.

METHODS

Subjects

The study protocol adhered to the tenets of the Declaration of Helsinki and was approved in advance by the Institutional Review Board of the University of California, San Diego. Healthy adults were recruited. Explanation of the nature and possible risks of the study was provided to each subject prior to obtaining written informed consent.

Equipment

Variations in transcranial ultrasonic time-of-flight were measured using the pulsed phase locked loop (PPLL) technique originally developed at NASA Langley Research Center and implemented by Luna Innovations (EN-TACT®, Roanoke, VA) (6). Principle of the PPLL technique has been described previously (14). Briefly, a transducer probe transmitted an

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ultrasound tone through the cranium, the ultrasound wave reflected off the inner surface of the opposite side of the skull, and the echo was received back by the transducer. Reflections from objects in the acoustic pathway were registered (e.g., x-axis as time and y-axis as amplitude on an oscilloscope). An operator determined the best reflection signal as the lock point. A change in the cranial diameter produced a phase shift between the emitted ultrasound signal and the echo received. The PPLL algorithm compared the phases and altered the ultrasound output voltage in proportion to the change of the cranial diameter. Thus, a "loop" of operations included the ultrasound generator, the echo, and the phase comparator with the feedback of the phase difference to the ultrasound generator. One loop took approximately 0.5 ms before the next loop was initiated. Monitoring the PPLL output voltage provided a continuous recording of cranial oscillation, including the pulsations caused by heartbeat and arterial blood pressure. Using the PPLL technique, continuous recording of the ultrasonic time-of-flight across the temporal bones produced a waveform that was positively correlated ($r^2 = 0.882$) with the real ICP waveform recorded by an intraparenchymal pressure transducer in neurological patients (14). The two waveforms corresponded to the cardiac and respiratory cycles.

Procedure

For the present study, an ultrasound transducer operating in the pulse-echo mode was placed on the middle forehead above the eyebrow line. The location provided a relatively flat and smooth surface for the transducer. The transducer with ultrasound gel (Parker Laboratories, Fairfield, NJ) was secured using a head frame and an elastic bandage to avoid slipping during the experiment. The experimental setup was verified for generating ultra-sound waveforms while the subject was standing up. The settings were set to produce a 1-MHz ultrasonic tone burst with a repetition frequency of 1 kHz. After choosing an appropriate echo, the phase-locking algorithm was applied to record the changes in the ultrasonic time-of-flight. A clinical blood pressure cuff was placed on the upper arm. Subjects then moved to a tilt table with the ultrasound transducer and blood pressure cuff in place.

Once on the tilt table, the subject's body was tilted to one of five randomly chosen angles: +30°, 0°, −30°, −60°, or −90°. Previous studies documented that ICP changed approximately 1 mmHg for every 10° change in head position (11). Thus, these body tilt angles may produce an ICP range of approximately −3 mmHg to +9 mmHg compared to the ICP in the lateral decubitus body position. Considering the average of ICP in healthy decubitus individuals is about 12 mmHg (1), the experimental model provided an ICP range of 9 to 21 mmHg. This range covers the slightly low ICP associated with glaucoma and the relatively high ICP in astronauts showing visual abnormalities using their lumbar cerebrospinal fluid (CSF) pressures as the guide (1, 7).

After 1 min at the first tilt angle, the subject's ultrasonic time-of-flight waveform was monitored for 1 min and saved. A single measurement of blood pressure and heart rate was taken. Then the subject's body was transitioned to the tilt angle of +30° and remained there for a 1-min equilibrium period prior to the next body tilt. The tilt angle was chosen at random and the experimental procedure was repeated until data from all five body tilt positions were collected. After completion of the first set of data collections, the subject

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waited upright for approximately 15 min before a second set of data collections with various body tilts according to the procedure outlined above.

Data Analysis

The pulse amplitude from the ultrasonic time-of-flight waveform at each body tilt angle was determined. The first 6-s recording was bandpass filtered over a frequency range of 0.25 to 10 Hz. The first second of the waveform was truncated in order to remove low-frequency artifacts. An autocorrelation function was applied to the waveform to measure periodicity. Timing of the central peak of the autocorrelation signal to the next peak from the center provided a factor that represents the periodicity in the waveform. For a valid signal with no significant motion artifacts, the periodicity of the waveform should match with the heart rate. This process was repeated for a new 6-s interval of data with the start time 1 s after the first interval. In total, 54 waveform slices were analyzed for each 1-min recording. All the waveform slices obtained for a given tilt angle were compared to the heart rate recorded. Slices in which the periodicity did not occur within the heart rate ±10% were rejected. The pulse amplitudes from all valid waveform slices at the same tilt angle from the two sets of data collections were averaged and used for subsequent statistical analysis.

Repeated-measures ANOVA and post hoc Bonferroni t-test with multiple paired comparisons were used to determine a difference in the pulse amplitudes among the five body tilt angles. Since the mean blood pressure, pulse blood pressure (systolic pressure minus diastolic pressure), and heart rate may also change due to different body tilts, repeated-measures ANOVA and post hoc Bonferroni t-test were performed to examine the effects of tilt angles on these cardiovascular parameters. Linear regression was used to examine the correlation between tilt angle and pulse amplitude using data obtained from all subjects. Linear regression was also used to examine individual change patterns of pulse amplitude due to the increase of head-down tilt angle using data obtained from each subject. It is possible that tilt angle, mean blood pressure, and heart rate were interrelated in ICP regulation and consequently the magnitude of pulse amplitude. Multiple regression analysis was performed to investigate the joint effect of explanatory variables of tilt angle, mean blood pressure, and heart rate on the dependent variable of pulse amplitude. Results of statistical analyses were considered significant when $P < 0.05$.

RESULTS

There were 15 male subjects and 1 female subject who enrolled in this study. All participants completed the experimental procedure with no adverse effects. However, valid data was not obtained from one male subject at the −90° tilt angle and this subject was excluded from data analyses. The remaining 15 subjects had an age of 28.2 ± 13.9 (mean ± SD), height of 175.9 ± 7.3 cm, weight of 74.3 ± 10.5 kg, and body mass index of 23.9 ± 2.5 $kg \cdot m^{-2}$.

Fig. 1 summarizes the pulse amplitudes of the transcranial ultrasound waveforms at the five body tilt angles of −90°, −60°, −30°, 0°, and +30°. Repeated-measures ANOVA indicated a significant difference in the pulse amplitudes among the five tilt angles [$F(4,56) = 10.595$, $P < 0.001$]. Subject-to-subject variation accounted for 50.5% of total variation and the within-subject variation counted for 49.5% of total variation. Post hoc Bonferroni *t*-test showed that the pulse amplitude recorded at the −90° tilt angle was significantly larger than the pulse amplitudes at the −60° [$t(56) = 3.074$, $P = 0.032$], −30° [$t(56) = 3.249$, $P = 0.020$], 0° [$t(56) = 3.973$, $P = 0.002$], and +30° [$t(56) = 6.431$, $P < 0.001$] tilt angles. The pulse amplitude at the +30° tilt angle was significantly smaller than those recorded at the −60° [$t(56) = 3.357$, $P = 0.014$] and −30° [$t(56) = 3.182$, $P = 0.024$] tilt angles. No statistically significant difference appeared in the pulse amplitudes between any two tilt angles of −60°, −30°, and 0°.

Linear regression analysis showed a negative correlation between the tilt angle and the pulse amplitude for data collected from all subjects ($N = 75$, $r^2 = 0.191$, $P < 0.001$), indicating that a larger head-down body tilt angle was associated with a larger pulse amplitude of transcranial ultrasound waveform (Fig. 2). The regression line equation is: pulse amplitude = (1.158 − 0.01023 × tilt angle) × 10^{-4} voltage. For each individual subject, the regression line of pulse amplitude on tilt angle showed a negative slope (ranged from −0.02819 to −0.00110). None of the individual slopes was statistically different from the slope of the above regression line equation.

To determine if changes in the pulse amplitude of transcranial ultrasound waveform were closely associated with altered cardiovascular parameters, the relationships between the tilt angle and mean arterial blood pressure, pulse blood pressure, and heart rate were analyzed. Repeated-measures ANOVA indicated a significant difference in the mean blood pressures [$F(4,56) = 5.059$, $P = 0.001$] (Fig. 3) and in the heart rates [$F(4,56) = 9.498$, $P < 0.001$] (Fig. 4) among the five tilt angles, but no significant difference in the pulse blood pressures [$F(4,56) = 1.340$, $P = 0.267$]. The post hoc Bonferroni *t*-test showed a difference in mean blood pressure between the +30° tilt angle and the tilt angle of −60° [$t(56) = 4.051$, $P = 0.002$], −30° [$t(56) = 3.209$, $P = 0.022$], or 0° [$t(56) = 3.560$, $P = 0.008$]. A difference in the heart rate appeared between the +30° tilt angle and the tilt angle of −90° [$t(56) = 5.052$, $P < 0.001$], −60° [$t(56) = 4.695$, $P < 0.001$], −30° [$t(56) = 5.126$, $P < 0.001$], or 0° [$t(56) = 4.472$, $P < 0.001$]. There was no significant difference in mean blood pressure or heart rate between any two of the tilt angles of −90°, −60°, −30°, or 0°.

Using multiple regression, the analysis of variance showed that at least one of the explanatory variables of tilt angle, mean blood pressure, and heart rate was significantly correlated with the pulse amplitude ($r^2 = 0.206$, $P = 0.001$). The multiple regression equation is: pulse amplitude = (1.275 − 0.011 × tilt angle − 0.003 × mean blood pressure + 0.002 × heart rate) × 10^{-4} voltage. Table I shows that only the correlation between head-down tilt angle and enlarged pulse amplitude was significant after adjusting for other explanatory variables.

DISCUSSION

The observation of a posture-dependent increase in the pulse amplitude of transcranial ultrasonic time-of-flight waveform in the anterior-posterior skull direction is consistent with previous observation of transcranial ultrasonic time-of-flight waveform between the two temporal bones using the PPLL technique (12). Both increases in the pulse amplitude may reflect increased ICP. The pulse amplitude of the ICP waveform is known to correlate positively with mean ICP level in head-injured patients (2) and the ultrasonic time-of-flight waveform over the temporal bones is positively correlated with the ICP waveform (14). Although experimental data show a significant subject-to-subject variation (approximately half of the total variation) due to individual ICP response to the body tilt plus the variation in the response of cranial diameter to the ICP pulsation, a significant linear relationship appears between the body tilt angle and the pulse amplitude of the anterior-posterior transcranial ultrasound waveform. Based on the reported equation between the change in the ultrasound travel distance and the output voltage when using the PPLL technique (13), the calculated change of intracranial diameter in the anterior-posterior skull direction is approximately 0.53 μm between the +30° to −90° tilt angles (1.227×10^{-4} voltage; Fig. 2). This smaller skull expansion compared to the transverse skull expansion between the temporal bones is probably due to the relatively thicker frontal and occipital bones. Nevertheless, the signal-to-noise level of ultrasound echo obtained in the anterior-posterior direction is sufficiently strong to show a significant correlation between the tilt angle and pulse amplitude.

Visual abnormalities that appeared in the seven astronauts include optic disc edema, globe flattening, choroidal folds, decreased near vision, and other anatomical findings (7). Lumbar punctures performed in four astronauts showed moderate elevations of CSF pressure to 16–21 mmHg after return to Earth for 12–66 d. Elevated ICP under microgravity is considered the leading cause and an obstruction in cerebral blood outflow described as space obstructive syndrome may also be involved (15). Similar visual abnormalities are also observed in patients with idiopathic intracranial hypertension or in patients with postsurgical hypotony, showing an extremely low intraocular pressure (IOP). Physiological pressure balance within the optic nerve head, where subarachnoidal and intraocular forces interact, may have shifted in favor of the intracranial force, leading to the visual abnormalities. In another development, investigators reviewed 1985 to 2007 Mayo Clinic records of neurological patients receiving lumbar punctures and found a correlation between primary open-angle glaucoma and low lumbar CSF pressure that was used as a representative of ICP. The average lumbar CSF pressure in the glaucoma patients was approximately 3 mmHg lower than the controls, supporting the concept that a high translaminar pressure difference (IOP minus ICP) within the optic nerve head is a major risk factor for glaucoma.

Determination of translaminar pressure difference requires data of IOP and ICP. Various techniques are available for relatively accurate IOP measurements. However, an accurate ICP reading can only be obtained by direct intracranial catheterization or by lumbar puncture, usually performed in a lateral decubitus body position, which severely limits the use in nontherapeutic research. Therefore, surrogate measures can be useful for noninvasive ICP investigations. Our experimental data were obtained in the anterior-posterior skull direction that is closely aligned with the orientation of retrolaminar subarachnoid space to the optic nerve head. Experimental results may be sufficiently related to the ICP on the optic nerve head. One may speculate that a similar posture-related ICP change may cause a bigger movement of the optic nerve head because of its relatively soft structure compared to the adjacent frontal bone if little compartmental change in the CSF pressure occurs around the optic nerve head (5). Considering the significant subject-to-subject variation, a preferred application of this surrogate measure should only include data comparison within a subject, such as monitoring the same individual before clinical appearance of ocular damage. In addition, baseline measurement of absolute ICP using a valid method may be desirable.

Body tilts also alter mean blood pressure and heart rate. For most head-down tilts from the +30° tilt angle, mean blood pressure decreases and pulse amplitude of the transcranial ultrasound waveform increases. Data also show no difference in mean blood pressure or heart rate between the 0° tilt angle and the −90° head-down tilt angle in contrast to the increase in pulse amplitude. Although variations in the cardiovascular parameters may influence the transcranial ultrasonic time-of-flight waveform in the experimental model, there is no direct, parallel relationship between the change of pulse amplitude and the change of mean arterial blood pressure or heart rate. A direct, parallel relationship may be regarded as a significant confounding factor for the experimental results. Results of multiple regression analysis confirm that mean blood pressure and heart rate are not significant explanatory variables for the observed changes in pulse amplitude.

The present experimental setup only covered an ICP range of approximately 9 to 21 mmHg. Whether or not the observed correlation is valid between the pulse amplitude of transcranial ultrasound waveform and a higher or lower ICP level requires further study. Tilt angle above +30° was not used in the present study since pilot data indicated that the ultrasound signals at higher head-up tilt angles were noisier than those observed in the experiment. It is known that the vertical upper body position (e.g., +90°) keeps the hydrostatic indifferent point between the C-6 and T-5 zones of the spinal cord, and the corresponding CSF pressure behind the frontal bone may be negative or close to zero (8). Cerebrospinal fluid in the local cisterns and cerebral ventricles may be compartmentalized and affect the quality of the transcranial ultra-sound signals (5).

The significant correlation of the ultrasonic time-of-flight waveform to the ICP waveform suggests that other techniques of waveform analyses developed for invasive ICP monitoring may be applicable to our experimental data. For example, in addition to an increase of pulse amplitude, rounding of the waveform shape may occur as ICP increases, reflecting a decrease of intracranial compliance (14). Intracranial compliance shows the pressure-volume relationship for the transmission of arterial blood pressure waves to ICP waves. When intracranial compliance is reduced, an increase in ICP transfer efficiency may be higher in the low-frequency components and less in the high-frequency components, leading to rounder waveforms. However, the frequency components of ICP waveform are complex (2). Given a possible more complex relationship between the frequency components of ICP waveforms and the shape of the transcranial ultrasonic time-of-flight waveforms, preliminary analysis of our experimental data did not offer a value of using the rounding of the waveforms as an index for the intracranial force.

In conclusion, the present study shows a significant negative correlation between the pulse amplitude of the anterior-posterior transcranial ultrasonic time-of-flight waveform and head-down, whole-body tilt that increases ICP. More research is warranted to explore usage of this surrogate measure of intracranial force on the optic nerve head in order to advance our knowledge of the cause for ophthalmic abnormalities during microgravity exposure and in glaucoma pathogenesis.

ACKNOWLEDGMENTS

This study was supported in part by the U.S. Army Medical Research and Materiel Command Contract W81XWH-09-C-0107 and NASA grant NNX12AL66G. John E. Lynch, Ph.D., was an employee of Luna Innovations.

REFERENCES

1. Berdahl JP, Yu DY, Morgan WH. The translaminar pressure gradient in sustained zero gravity, idiopathic intracranial hypertension, and glaucoma. Med Hypotheses 2012; 79:719–24. [PubMed: 22981592]
2. Contant CF, Jr, Robertson CS, Crouch J, Gopinath SP, Narayan RK, Grossman RG. Intracranial pressure waveform indices in transient and refractory intracranial hypertension. J Neurosci Methods 1995; 57:15–25. [PubMed: 7791362]
3. Hargens AR, Richardson S. Cardiovascular adaptations, fluid shifts, and countermeasures related to space flight. Respir Physiol Neurobiol 2009; 169 (Suppl. 1):S30–3. [PubMed: 19615471]
4. Keil LC, McKeever KH, Skidmore MG, Hines J, Severs WB. The effect of head-down tilt and water immersion on intracranial pressure in nonhuman primates. Aviat Space Environ Med 1992; 63:181–5. [PubMed: 1567318]
5. Killer HE, Jaggi GP, Flammer J, Miller NR, Huber AR, Mironov A. Cerebrospinal fluid dynamics between the intracranial and the subarachnoid space of the optic nerve. Is it always bidirectional? Brain 2007; 130:514–20. [PubMed: 17114796]
6. Lynch JE, Blaker DM, Colatosti DJ, inventors. Luna Innovations Incorporated, assignee. Digital pulsed phase locked loop. U.S. Patent 7,513,160; 2009 4 7.
7. Mader TH, Gibson CR, Pass AF, Kramer LA, Lee AG, et al. Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight. Ophthalmology 2011; 118:2058–69. [PubMed: 21849212]
8. Magnaes B Body position and cerebrospinal fluid pressure. Part 2: clinical studies on orthostatic pressure and the hydrostatic indifferent point. J Neurosurg 1976; 44:698–705. [PubMed: 1271090]
9. Michaeli D, Rappaport ZH. Tissue resonance analysis; a novel method for noninvasive monitoring of intracranial pressure. Technical note. J Neurosurg 2002; 96:1132–7. [PubMed: 12066918]
10. Popovic D, Khoo M, Lee S. Noninvasive monitoring of intracranial pressure. Recent Patents on Biomedical Engineering 2009; 2:165–79.
11. Rosner MJ, Coley IB. Cerebral perfusion pressure, intracranial pressure, and head elevation. J Neurosurg 1986; 65:636–41. [PubMed: 3772451]
12. Ueno T, Ballard RE, Macias BR, Yost WT, Hargens AR. Cranial diameter pulsations measured by non-invasive ultrasound decrease with tilt. Aviat Space Environ Med 2003; 74:882–5. [PubMed: 12924766]
13. Ueno T, Ballard RE, Shuer LM, Cantrell JH, Yost WT, Hargens AR. Noninvasive measurement of pulsatile intracranial pressure using ultrasound. Acta Neurochir Suppl 1998; 71:66–9. [PubMed: 9779147]
14. Ueno T, Macias BR, Yost WT, Hargens AR. Noninvasive assessment of intracranial pressure waveforms by using pulsed phase lock loop technology. J Neurosurg 2005; 103:361–7. [PubMed: 16175869]
15. Wiener TC. Space obstructive syndrome: intracranial hyper-tension, intraocular pressure, and papilledema in space. Aviat Space Environ Med 2012; 83:64–6. [PubMed: 22272520]

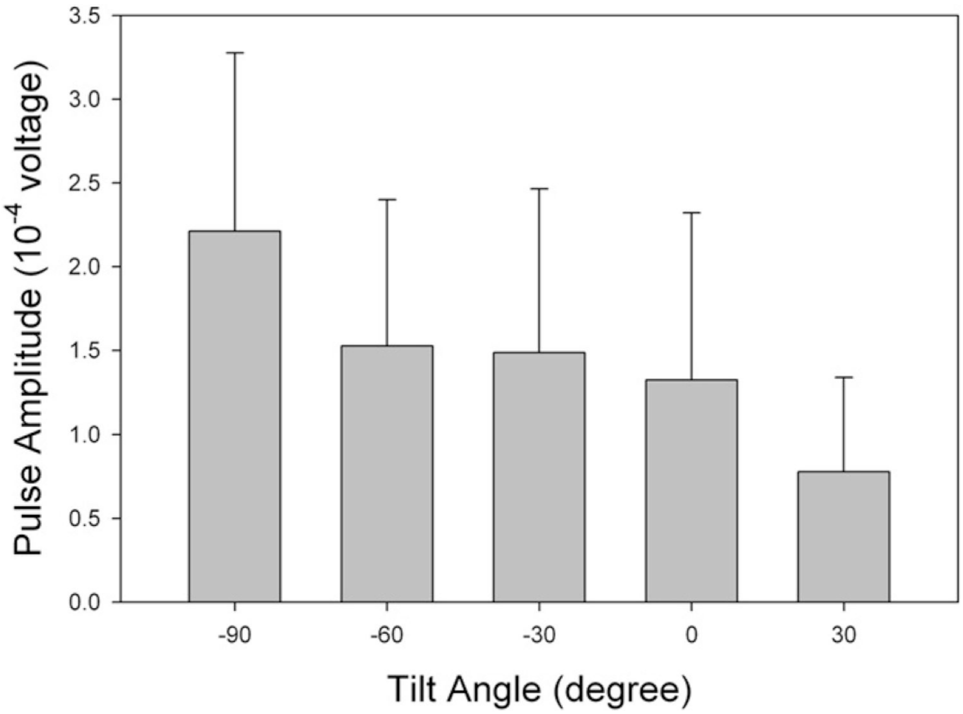

Fig. 1.
Mean pulse amplitudes of transcranial ultrasonic time-of-flight waveform at five different body tilt angles. Error bars represent SD (N = 15). Pulse amplitudes are shown in the recorded voltages using the pulsed phase locked loop technique.

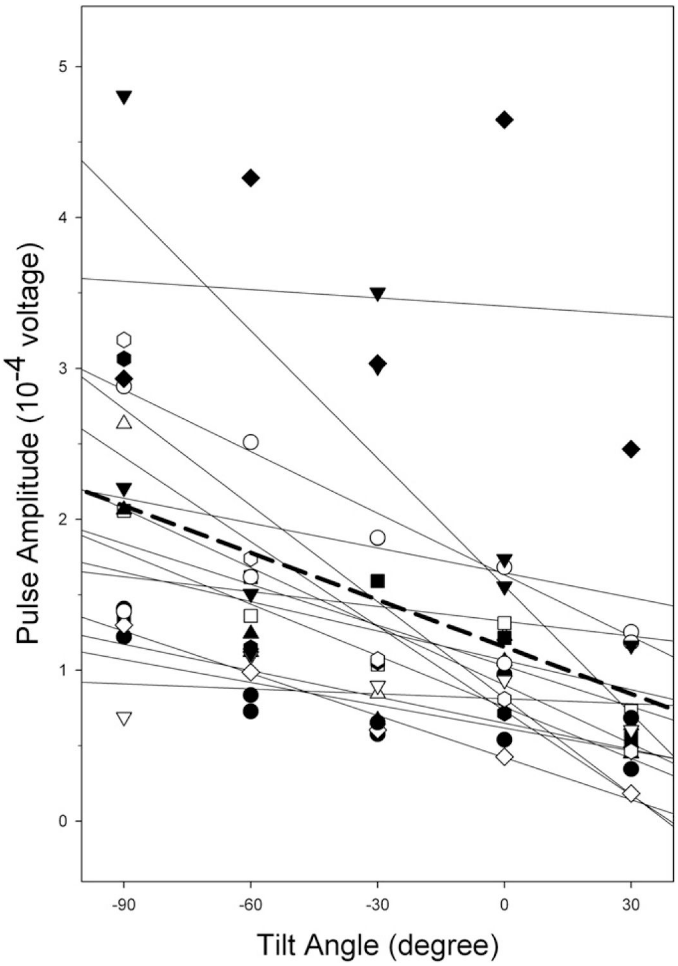

Fig. 2.

Scatter plot showing the relationship between pulse amplitude and tilt angle. Linear regression analysis indicates a negative correlation using data collected from all subjects (the dashed line). Individual regression lines of pulse amplitude on tilt angle using data collected from each subject all show a negative slope (15 solid lines).

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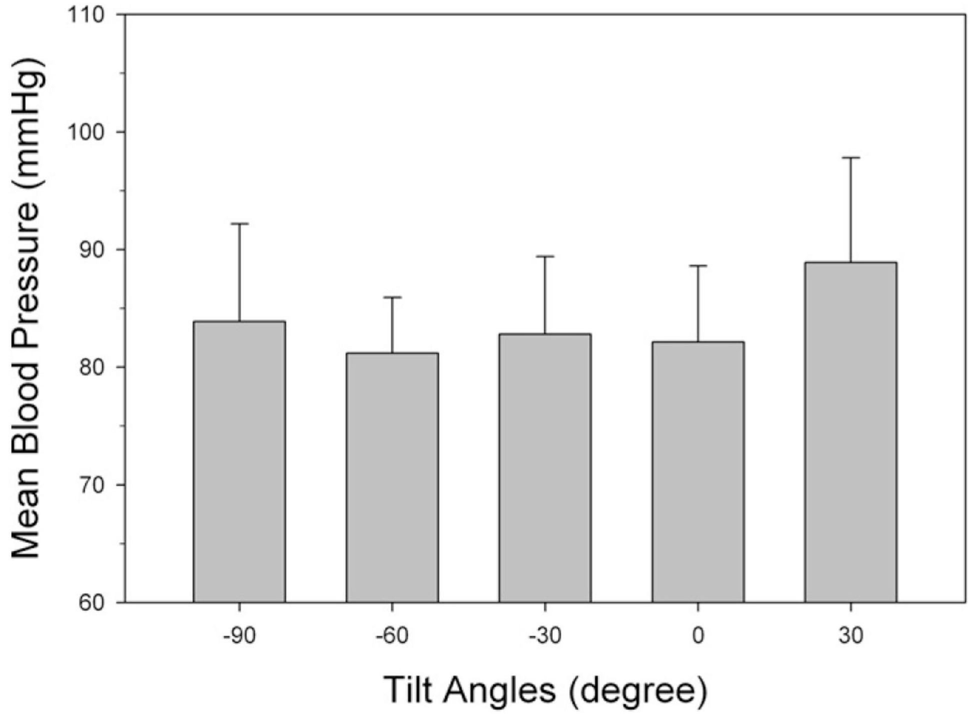

Fig. 3.
Mean blood pressures at five different body tilt angles. Error bars represent SD (N = 15).

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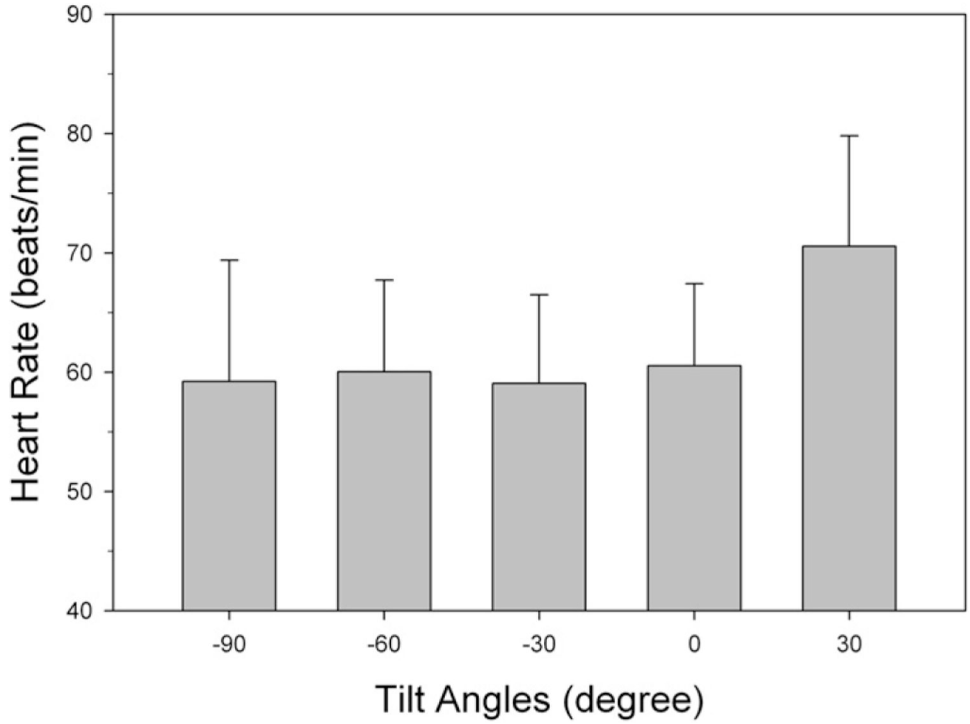

Fig. 4.
Mean heart rates at five different body tilt angles. Error bars represent SD (N = 15).

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TABLE I.

MULTIPLE REGRESSION ANALYSIS OF PULSE AMPLITUDE OF TRANSCRANIAL ULTRASONIC TIME-OF-FLIGHT WAVEFORM.

Variable	Parameter Estimate	Standard Error	95% Confidence Interval	*t*	*P*-Value
Intercept (10^{-4} voltage)	1.275	0.772	−0.264 to 2.815	1.652	0.103
Title angle (degree)	−0.011	0.003	−0.016 to −0.006	−4.190	< 0.001
Mean blood pressure (mmHg)	−0.003	0.011	−0.025 to 0.018	−0.287	0.775
Heart rate (bpm)	0.002	0.012	−0.021 to 0.025	0.161	0.872