Jugular and Portal Vein Volume, Middle Cerebral Vein Velocity, and Intracranial Pressure in Dry Immersion

Philippe Arbeille; Paul Avan; Loïc Treffel; Kathryn Zuj; Herve Normand; Pierre Denise

BACKGROUND: The objective was to determine if short term exposure to dry immersion (DI) results in a cephalic fluid shift similar to what has been observed with spaceflight.

METHODS: Data were collected from 10 individuals at rest and during the first 2 h of dry immersion. Jugular vein (JV), portal vein (PV), and thyroid volume were measured using 3D echography. Middle cerebral vein velocity (MCVv) was determined using transcranial Doppler ultrasound. The cochlear response to audio stimulation was used to derive an estimate of intracranial pressure (dICP).

RESULTS: After 2 h of DI, there was a significant increase (mean $\pm$ SD) in JV (2.21 $\pm$ 1.10 mL), PV (1.05 $\pm$ 0.48 mL), and thyroid (0.428 $\pm$ 0.313 mL) volume. MCVv was also significantly increased with DI (3.90 $\pm$ 5.03 $cm \cdot s^{-1}$). There was no change in dICP with DI in part due to large individual variability. The range of dICP changes appeared to be related to MCVv, with participants with the largest increase in MCVv also showing increased dICP.

DISCUSSION: The results suggest that DI induces a significant cephalic fluid shift similar to what is observed with spaceflight. The increased thyroid volume suggests that cerebral tissue may also be subjected to similar fluid filtration, with implications for changes in intracranial pressure. However, despite all participants having an increase in JV and thyroid volume, only half showed an increase in dICP, suggesting that increased venous pooling alone is not sufficient to cause increased intracranial pressure.

KEYWORDS: venous volume, spaceflight, fluid shifts, dry immersion.

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The observation of vision problems experienced by some astronauts during long duration spaceflights onboard the International Space Station has led to the hypothesis that cephalic fluid shifts induced by the microgravity environment result in an increased intraocular pressure (IOP) and intracranial pressure. A recent study has provided support for this hypothesis, demonstrating an increase in intracranial pressure and IOP with cephalic fluid shifts induced by head-down tilt and a reduction in intracranial pressure and IOP when fluid was shifted away from the head using lower body negative pressure.[8] A 7-d head down tilt study also noted cephalic fluid shifts indicated by a significant enlargement of the jugular vein (JV), which was accompanied by an enlargement of the eye fundus vein and the presence of edema at the eye fundus level, but not an increase in IOP.[3]

Dry immersion (DI) has been proposed as method of mimicking the effects of microgravity exposure on Earth[18] with various durations of use (10 h to 28 d). During DI, the subject is seated in a semirecumbent position inside a water tank with bags used to separate the subject from the water so that the subject remains dry. The subject is submerged up to the neck level, with the water pressure on the body promoting the transfer of interstitial fluid into the vascular system and a total shift of fluid toward the cephalic area.[11,12] During the first 4 h of immersion, cardiac stroke volume has been found to increase, with peripheral vascular resistance, heart rate, and diastolic blood pressure all decreasing.[12] Plasma volume has been found to be

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significantly reduced after 1 d of DI, with further reductions seen after 3 d.[6,17] Currently, there are no published data on central or peripheral venous flow or pressure changes during the first hours of DI.

The purpose of the current study was to investigate changes in venous volume and flow during the initial hours of DI and to relate these potential changes to alterations in an otoacoustically derived estimate of intracranial pressure (dICP). As DI is expected to result in a fluid shift toward the head, we hypothesized that both the JV and the portal vein (PV) would increase in volume similar to what has been observed with spaceflight.[2] Additionally, it was hypothesized that the increase in JV volume would result in an increase in dICP and, consequently, an increase in middle cerebral vein velocity (MCVv). Finally, it was speculated that thyroid volume would also be increased, providing further indications of the effects of fluid shift on the cephalic organ.

METHODS

Subjects

Participating in this study were 10 healthy male subjects (age: 31.8 ± 4.1 yr, height: 178.8 ± 5.6 cm; weight: 74.8 ± 5.6 kg; body mass index: 23.6 ± 1.2). All participants were nonsmokers, were not taking medications or drugs, and were free of any pathology. The study design was established in accordance with the Declaration of Helsinki and was approved by the local ethics committee (CPP Sud-Ouest, France). Subjects were selected based on a normal clinical assessment consisting of a detailed medical history, physical examination, an electrocardiogram, general blood screening, and urine analyses. Each participant gave written informed consent before participation in the study.

Equipment

JV volume was measured using 3D ultrasound (Toshiba, Applio 400, Paris, France). A 7-10 MHz 3D probe was located at the anterior part of the neck with the transducer in vertical position and the probe body in contact with the collar bone (**Fig. 1A** and **Fig. 1B**). Minimal pressure was applied to the skin by the probe to avoid compressing and changing the JV cross section. The sonographer used a single sweep to scan the JV and manually identified the contours of the vein in a long and short axis plane. The ultrasound system then reconstructed the volume of the JV and displayed the calculated volume in cm^3. With the probe in a horizontal orientation, the same procedure was used to determine the volume of the thyroid right lobe (**Fig. 1C**). During the volume measurements, the sonographer reviewed the contouring selected by the ultrasound system and made adjustments as necessary.

Using the same ultrasound system (Toshiba, Applio 400), 2D images were acquired for the measurement of left ventricular end diastolic volume (LVDV), left ventricular end systolic volume (LVSV), common carotid artery (CCA) blood flow, and the cross-sectional area of the PV. For the measurement of the PV, a 3.5-MHz probe was located at the intersection of the vertical mammary and transverse xiphoid lines and oriented with a 45° counterclockwise rotation from the vertical. The main trunk of the PV was displayed on a long axis view and its diameter measured. Volume of the PV was then calculated assuming a 4-cm cylindrical length of the vein. A 3.5-MHz phased array probe was used to determine LVDV and LVSV with cardiac stroke volume (SV) calculated as the difference between these values. CCA blood velocity and average diameter were determined using a 7–10 MHz linear probe. Blood flow in the CCA was then calculated as the product of blood velocity and vessel cross-sectional area calculated from the measurement of vessel diameter.

Intracranial veins are not usually investigated in adults and are not easy to visualize using transcranial ultrasound. Therefore, we were required to develop a method to find and record the intracranial venous Doppler signal using transcranial echography (Toshiba, Applio 400). To determine MCVv, a 1.5-MHz phased array probe was located over the temporal window and adjusted to clearly visualize the middle cerebral artery (MCA). The area around the MCA was then searched to determine the best location for detecting venous blood velocity. The Doppler filter was lowered to improve the detection of low venous blood velocities and the sample volume increased to help facilitate the detection of any venous flow in the vicinity of the MCA (**Fig. 2**).

An estimate of intracranial pressure (dICP) was determined using the cochlear response to auditory stimulation. The cochlear aqueduct is a narrow channel connecting the subarachnoid and intralabyrinthine spaces. Through this communication, cerebrospinal fluid pressure variations are transmitted to the intralabyrinthine space and modify the impedance of the ear. Distortion-product otoacoustic emissions (DPOAE) are sounds emitted by cochlear sensory cells in response to sonic stimulation. Cochlear microphonic potentials express the electrophysiological activity of cochlear sensory cells. At 1 kHz, the phase of DPOAE and cochlear microphonic potentials vary per the impedance of the ear, providing an estimate of intracranial pressure variations.[14]

Procedure

This experiment consisted of a 3-d ambulatory control period followed by DI. During DI, subjects remained in a semirecumbent position in a controlled, thermoneutral (33 ± 0.5°C) bath. Waterproof bags were used to contain the bath water and separate the subject from the liquid, maintaining a dry environment. Measurements were conducted before DI (PRE) and after 2 h of DI with the participant in the DI tank. Previous work has reported that plasma volume is decreased by 16–30% after 1 d of DI.[6] Therefore, the current study investigated potential fluid shifts during the first few hours of DI when the vascular changes due to the redistribution of fluid were expected to be greatest. All PRE measurements were conducted with the subjects in a semirecumbent position similar to the position during DI.

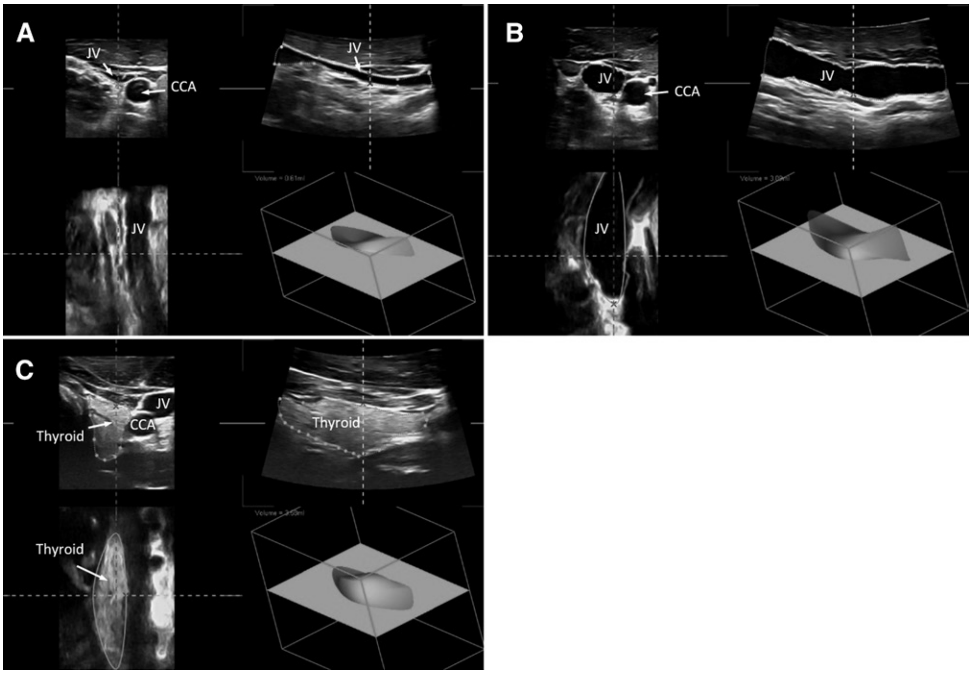

Fig. 1. Images of the 3D ultrasound assessments of JV volume A) PRE and B) after 2 h of DI, and C) thyroid volume after 2 h of DI. The 3D reconstructions (bottom right in each image) were computed using 2D images in the transverse (top left), sagittal (top right), and frontal (bottom left) planes.

Additionally, all study measurements were conducted in a quiet room at a temperature of ~25°C.

Statistical Analysis

The effects of DI were assessed using a one-way repeated measures ANOVA with Tukey post hoc testing (SigmaPlot 12.5, Systat Software Inc, Chicago, IL). The Pearson moment correlation coefficient was calculated to determine potential relationships between JV volume and MCVv, and the change with DI in dICP, JV volume, and MCVv. For all tests, significance was set at $P < 0.05$, with group results presented as mean ± SD.

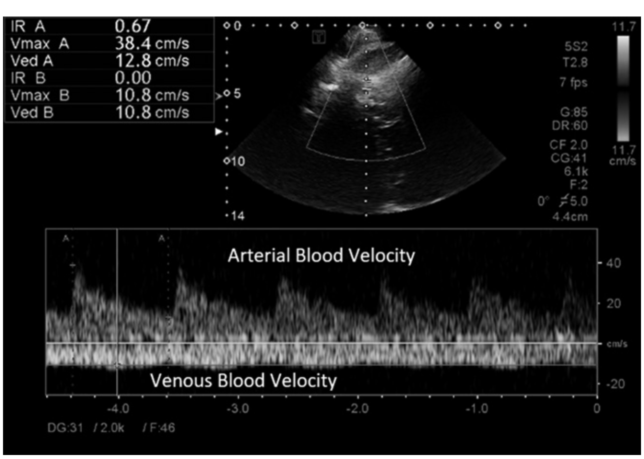

Fig. 2. An example of the middle cerebral vein assessment using transcranial Doppler. For the measurement of MCVv, the Doppler gate was first positioned to obtain middle cerebral artery velocity (top of Doppler spectrum) and adjusted slightly until the venous velocity (bottom of the Doppler spectrum) was clearly visible for assessment.

RESULTS

Cardiac ultrasound measurements during the first few hours of DI showed no change in LVDV [PRE: 81.90 ± 18.64 mL, DI: 78.83 ± 7.60 mL, $F(1,8) = 0.201$, $P = 0.67$], a significant reduction in LVSV [PRE: 35.63 ± 10.25 mL, DI: 30.25 ± 7.61 mL, $F(1,7) = 8.328$, $P = 0.023$], but no significant change in SV [PRE: 44.01 ± 18.37 mL, DI: 48.11 ± 6.78 mL, $F(1,7) = 0.34$, $P = 0.58$]. Blood flow in the CCA was significantly reduced during the first hours of DI [PRE: 349.67 ± 59.22 $mL \cdot min^{-1}$, DI: 301.00 ± 38.30 $mL \cdot min^{-1}$, $F(1,8) = 16.24$, $P = 0.004$], with no change in CCA diameter [PRE: 0.606 ± 0.046 cm, DI: 0.613 ± 0.041 cm, $F(1,8) = 1.45$, $P = 0.263$].

With DI, there was an increase in JV volume (**Fig. 3A**) for all subjects, with a mean increase of 2.21 ± 1.10 mL [$F(1,9) = 40.22$, $P < 0.001$]. PV volume was also increased (**Fig. 3B**) for all subjects, with a mean change of 1.05 ± 0.48 mL [$F(1,9) = 48.08$, $P < 0.001$]. On average MCVv was increased 3.90 ± 5.03 $cm \cdot s^{-1}$ [$F(1,8) = 5.42$, $P = 0.048$], but there was a large degree of individual variability in response (**Fig. 3C**), with several subjects showing little or no change in MCVv. Ultrasound measurements showed a 0.43 ± 0.31 mL increase in thyroid right lobe volume (**Fig. 3D**) within the first few hours of DI exposure [$F(1,9) = 18.732$, $P = 0.002$]. Overall, there was a significant correlation (**Fig. 4**) between JV volume and MCVv [$r(18) = 0.766$, $P < 0.001$], with this relationship mainly being driven by the relationship between JV volume and MCVv during DI [$r(9) = 0.93$, $P < 0.001$].

Technical issues resulted in dICP being assessed in only seven participants. A mean change of 34 ± 125 mmH_2O was found for dICP, but this was not statistically significant due to the large variability in individual response [$t(6) = 0.725$, $P = 0.496$]. Similarly, the changes in dICP were not correlated with the change in MCVv [$r(7) = 0.510$, $P = 0.242$] or JV volume [$r(7) = 0.278$, $P = 0.546$]. **Table I** reports the individual changes in dICP and MCVv with dry immersion.

DISCUSSION

Earth-based spaceflight simulation studies have primarily used head-down bed rest (HDBR) as a model of microgravity exposure due, in part, to fluid shifts toward the cephalic and thoracic regions. The use of DI has been proposed as an alternative model of microgravity exposure; however, studies investigating

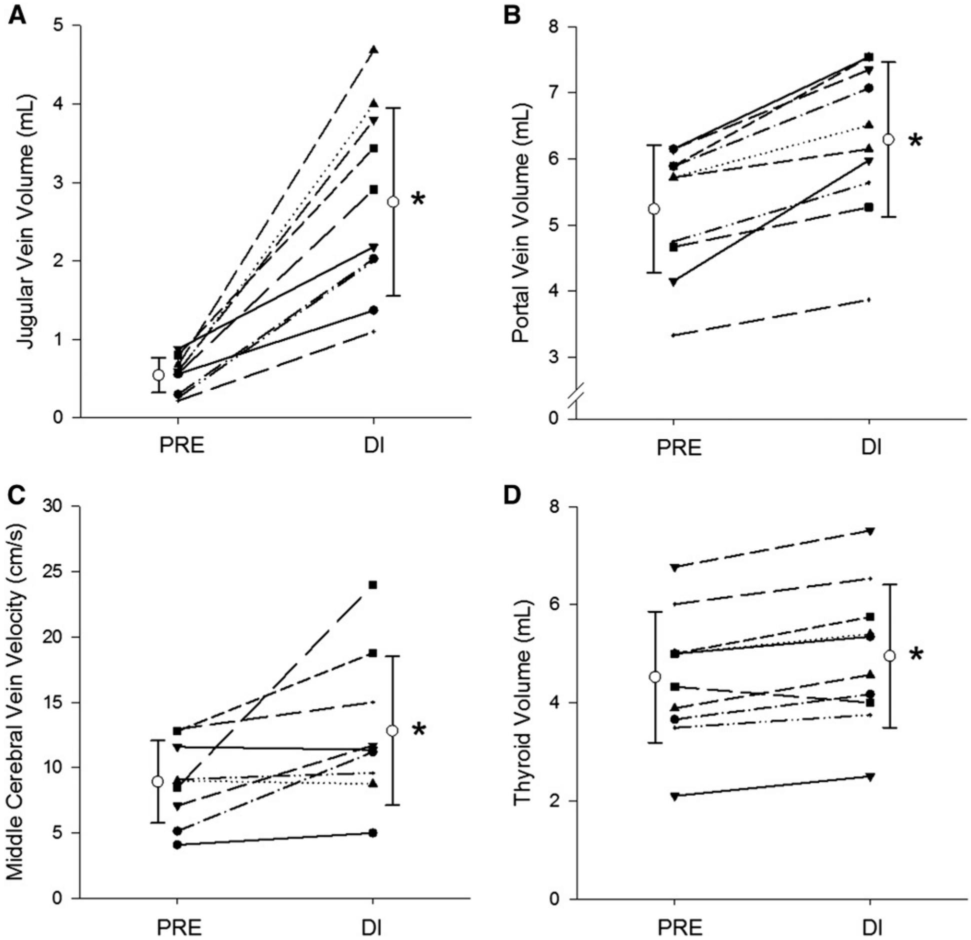

Fig. 3. Graphs showing the individual (smaller symbols and connecting lines) and mean (white circles ± SD) measurement results of A) JV volume, B) PV volume, C) MCVv, and D) thyroid right lobe volume PRE and after 2 h of DI. * $P < 0.05$.

fluid shifts and resulting hemodynamic response are limited. The current study used ultrasound measurements to evaluate cephalic fluid shifts during the first hours of DI exposure. Consistent with the hypothesis, DI resulted in increased JV volume, PV volume, and thyroid volume, which all suggest significant fluid shifts toward the head during the first hours of DI.

With DI, an increase in PV volume was found, suggesting increased blood pooling within the splanchnic region. This result is consistent with a study of HDBR where an increase in PV diameter was found after 4 h of HDBR.[5] Additionally, an increase in PV volume has been recently reported during long-duration spaceflight.[2] Similar changes in PV dimensions with HDBR, DI, and spaceflight suggest that all three conditions may result in splanchnic blood pooling due to fluid redistribution, potentially supporting the use of DI as an alternative Earth-based analog to spaceflight.

Measurements of the JV have been used to determine cephalic fluid shifts, with HDBR and spaceflight causing an increase in JV volume with both HDBR[1,3,15] and spaceflight.[2,7] The observed increase in JV volume in the current study potentially suggests a similar change in fluid redistribution, leading to distention of the JV. However, the mechanisms of this increase in JV volume with DI may be different compared to HDBR or spaceflight.

Previous work has demonstrated that JV volume and blood flow change with alterations in posture. Work by Valdueza et al.[20] demonstrated that compared to a supine position, JV blood flow and cross-sectional area were much smaller in an upright posture. A commentary by Weiner[21] suggested that external pressure on the JV in an upright posture, potentially caused by the carotid artery and neck musculature, could be a potential mechanism for this reduction in flow and volume. Additionally, it was suggested that in a supine position, the force of gravity promotes the lateral translation of the jugular vein, allowing for an increase in JV volume and flow.[21] In a head-down position, as what is used with HDBR, the force of gravity would likely still result in translation of the JV, preventing impingement[21] and allowing for the observed increase in volume.[1,3,9,15] However, this does not translate into a further increase in flow, as recent work has demonstrated that with head-down tilt, the increase in JV volume is associated with a reduction in JV flow.[9] In the current study, it is unlikely that changes in external pressure on the JV contributed to the observed increase in volume as measurements were made with participants in the same body position with the same gravitational vector acting on the JV. Therefore, the increase in JV volume with DI is likely due to fluid shifts toward the cephalic area induced by compression of the water on the lower legs, abdomen, and lower thorax.

The observed increase in thyroid volume with DI further supports the hypothesis that DI results in cephalic fluid shift. Increased capillary filtration, leading to the development of edema, likely contributed to the increase in thyroid volume. Changes in capillary filtration at the level of the thyroid may also indicate a similar change in cerebral tissue, with implications for changes in intracranial pressure and cerebral blood flow. Cerebral edema has been demonstrated in an animal model of microgravity exposure, where 6 h of head-down tilt was found to result in increased capillary pressure in the head, increased facial edema, and histological changes in cerebral tissue.[16] Currently, it is unknown if DI results in cerebral edema, but the observation of increased thyroid volume does suggest the possibility.

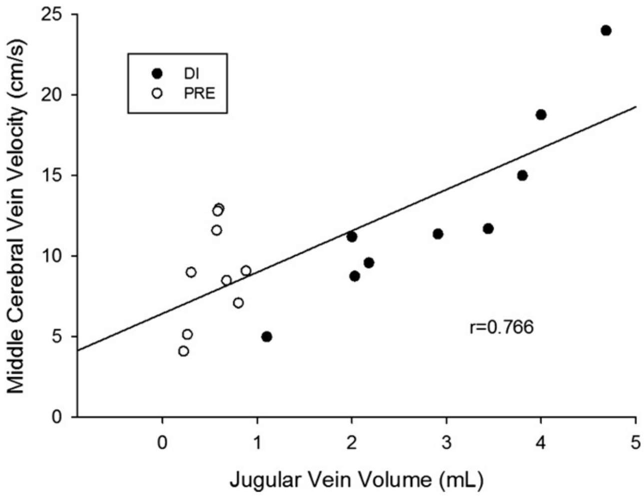

Fig. 4. Graph showing the relationship between MCVv and JV volume before (white circles) and after 2 h of DI (black circles).

The observed increase in MCVv was consistent with our hypothesis that cephalic fluid shifts would contribute to an increased external pressure on the cerebral veins, leading to an increase in blood velocity. As SV was not increased and CCA blood flow was reduced with DI, the MCVv flow would not have been due to increased cerebral arterial flow. The significant relationship between JV volume and MCVv with DI further support to the hypothesis of extracranial venous congestion being associated with increased external pressure on intracranial veins. Although not statistically significant, there also appeared to be a directional relationship between MCVv and dICP (Table I), where subjects who showed the greatest change in dICP also showed large increases in MCVv. Therefore, assuming either constant or reduced venous outflow from the cerebral circulation, the observation of increased MCVv would indicate compression of the veins. However, contrary to the study hypothesis, on average, dICP was not increased with DI.

Previous studies of head-down tilt have noted an increase in intracranial pressure,[10,13] leading to the hypothesis that intracranial pressure would be increased with DI. The lack of a significant change in dICP was surprising as nearly all subjects showed increased JV and thyroid volume, indicating cerebral fluid shifts. This result may suggest that cephalic fluid shifts alone are not sufficient to cause increases in intracranial pressure. Additionally, studies have shown no changes in cerebral edema[4] or cerebral spinal fluid production[19] despite observations of increased intracranial pressure, which further support the notion of multiple factors contributing to intracranial pressure changes.

Table I. Individual Changes in Intracranial Pressure and Middle Cerebral Vein Velocity with Dry Immersion.

SUBJECT	dICP (mmH_2O)	MCVv (cm · s^{-1})
S2	110	0.9
S3	−10	2.05
S4	195	4.6
S6	−190	−0.23
S8	−5	0.5
S9	15	−0.23
S10	125	15.5

Values show the individual responses for changes in derived intracranial pressure (dICP) and middle cerebral venous blood velocity (MCVv) with dry immersion. Although not statistically correlated due to the small sample size ($N = 7$), there appears to be a directional relationship where subjects with increased MCVv also showed increased dICP.

In addition to multiple factors potentially contributing to changes in intracranial pressure, technical limitations may also have led to the lack of change in dICP. The current study used DPOAE estimates of intracranial pressure. While this measure has been shown to relate to changes in intracranial pressure, it may not be sensitive enough to detect changes in intracranial pressure less than 12 mmHg.[22] This may provide a significant limitation as other work has only shown an increase in intracranial pressure of approximately 5 mmHg and 10 mmHg at 10° and 20° head-down tilt, respectively.[13] Additionally, a large degree of individual variability and a small sample size (seven participants) may have contributed to this estimate not reaching significance. Therefore, further study is needed to determine potential effects of DI on intracranial pressure.

Results from the current study demonstrate that 2 h of DI exposure results in significant fluid shifts toward the upper part of the body similar to what has been previously reported with spaceflight. PV and JV volumes were increased in all subjects, indicating venous pooling and potentially increased capillary filtration, leading to the observed increase in thyroid volume. Despite the consistent increase in thyroid volume and JV volume, dICP was not significantly different, with DI potentially suggesting that mechanisms other than venous pooling contribute to intracranial pressure with DI.

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