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Physiological adaptation of the jugular venous pulse during long-duration spaceflight

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Abstract

The jugular venous pulse (JVP) offers a non-invasive window into right atrial pressure. In microgravity, the serial JVP waveform during long-duration spaceflight had never been characterised. Using ECG-synchronised high-resolution ultrasound and a validated AI model, we quantified internal jugular vein cross-sectional area (IJV-CSA) throughout the cardiac cycle in four astronauts before and after flight, with in-flight measurements in one astronaut. Mean IJV-CSA fell significantly post-flight in three astronauts (ASTRO 0: from 0.723 ± 0.076 to 0.453 ± 0.061 cm^2, $p < 0.001$; ASTRO 2: −46.0%; ASTRO 3: −48.4%). The reduction in ASTRO 0 developed between the first and fifth month in orbit. Maximum CSA declined consistently with reduced central venous pressure. Pulsatile excursion, an index never previously reported in spaceflight, increased markedly (ASTRO 0: +105.0%, $p < 0.001$; ASTRO 2: +337.1%, $p < 0.001$), suggesting enhanced transmission of cardiac pressure waves towards the cerebral venous compartment in the absence of hydrostatic gradients. ASTRO 1 showed the opposite pattern (minimum CSA +42.5%, pulsatile excursion −60.3%, $p < 0.001$), probably due to IJV thrombosis, representing the third documented case in space medicine. The JVP waveform retains terrestrial morphology and ECG timing in microgravity. Whether JVP parameters predict venous thrombosis or relate to glymphatic function in long-term spaceflight warrants further studies.

Keywords Jugular venous pulse · Internal jugular vein · Microgravity · Spaceflight · Ultrasound · Venous thrombosis

Introduction

The jugular venous pulse (JVP) is the pressure waveform transmitted from the right atrium to the internal jugular vein (IJV). It consists of characteristic waves (a, c, v) and descents (x, y) synchronised with the cardiac cycle and provides a direct non-invasive window into right atrial and central venous pressure, reflecting preload, right heart function and volume status[1,2]. The a-wave corresponds to atrial contraction and therefore to the maximum cross-sectional area of the vein within the cycle; the x-descent corresponds to atrial relaxation during ventricular systole and therefore to the minimum cross-sectional area.

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An important physiological feature is that the JVP propagates retrograde (towards the brain), whereas blood flow is directed antegrade (towards the heart) (Fig. 1). Positive deflections of the waveform (a and v waves) correspond to the lowest blood flow velocities, while the negative descents (x and y) coincide with the highest velocities. This inverse relationship arises because the descents reflect the greater pressure gradient created by right atrial aspiration, which accelerates venous return[3]. The amplitude of the excursion between the a-wave and the x-descent (quantified here as pulsatile excursion) therefore expresses the extent to which cardiac pressure waves are transmitted towards the cerebral venous compartment; on Earth it is greater in the supine than in the sitting posture[4–6].

Accurate assessment of the JVP is particularly relevant in space medicine. During long-duration missions aboard the International Space Station (approximately five to six months in the present series), the absence of gravity induces a sustained cephalad fluid shift. This leads to IJV distension, altered flow patterns including stasis and retrograde flow, and an elevated risk of venous thrombosis [7,8].

We previously demonstrated that high-resolution B-mode ultrasound video of the pulsatile IJV, combined with ECG synchronisation and autocorrelation analysis, can accurately estimate central venous pressure non-invasively[9]. We further showed the feasibility of self-acquired ultrasound JVP assessment by astronauts in orbit, with accuracy comparable to or higher than that obtained on Earth[10,11].

Previous spaceflight studies have quantified the IJV from single-frame or single-phase acquisitions, from which the mean, minimum and maximum cross-sectional area within the cardiac cycle, and therefore the pulsatile excursion, cannot be derived [7,8]. Answering these questions requires the vein to be segmented on every frame of every clip, which is the reason for the automated approach adopted here.

Within the framework of the Drain Brain 2.0 project, sponsored by the Italian Space Agency, we characterised the physiological adaptations of the JVP during long-duration spaceflight and explored its potential role in the pathophysiology of the heart-to-brain circulatory axis.

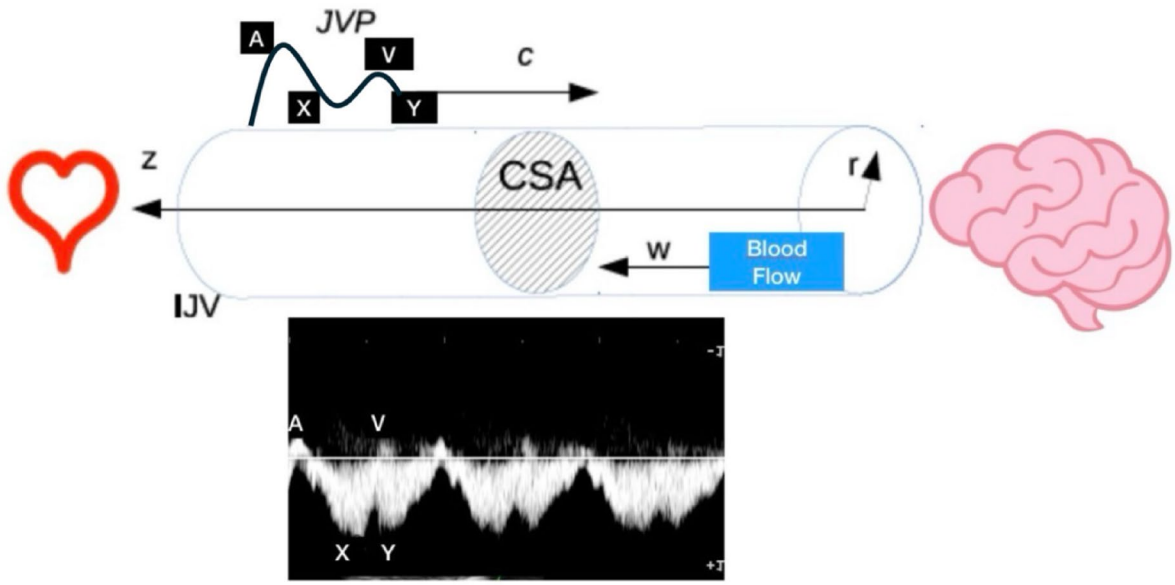


Fig. 1 Relationship between the JVP waveform (c) and the Doppler blood flow velocity in the IJV (w). Positive JVP peaks (a and v) correspond to the periods of lowest blood flow velocity, whereas the x and y descents correspond to peak flow velocity, owing to the increased right atrial suction. The pressure wave travels retrograde toward the brain, in the direction opposite to that of blood flow. This phenomenon is amplified in microgravity. Cited in the Introduction.

Results

Internal jugular vein cross-sectional area (IJV-CSA) was measured throughout the cardiac cycle in four astronauts before and after long-duration spaceflight, and at two in-flight time points just in one astronaut. A total of 3855 frames were segmented with the in-house convolutional pipeline described in the Methods. Participant characteristics and session timings are summarised in Table 1; the complete set of CSA, pulsatility and heart rate parameters is reported in Table 2.

Three astronauts (ASTRO 0, ASTRO 2 and ASTRO 3) showed a significant reduction in mean IJV-CSA at the early post-flight session (within one week of splashdown) compared with pre-flight values (Table 2). In ASTRO 0, mean IJV-CSA decreased from 0.723 ± 0.076 cm^2 pre-flight to 0.453 ± 0.061 cm^2 at post-flight 1 ($p < 0.001$) and remained lower at 0.466 ± 0.039 cm^2 at post-flight 2 ($p < 0.001$). Comparable significant reductions were observed in ASTRO 2 (−46.0%) and ASTRO 3 (−48.4%) at post-flight 1, with partial recovery by post-flight 2 (Table 2).

The only longitudinal in-flight series is that of ASTRO 0. In this astronaut the reduction in IJV-CSA was not yet apparent within the first week aboard the International Space Station, whereas at five months all measured IJV-CSA parameters were significantly reduced (Fig. 2). This trajectory describes a single participant and is not presented as a group finding.

In contrast, ASTRO 1 exhibited a significant increase in mean IJV-CSA, from 1.041 ± 0.096 cm^2 pre-flight to 1.243 ± 0.059 cm^2 at post-flight 1 (4 days after return) and to 1.732 ± 0.028 cm^2 at post-flight 2 (Table 2). This increase was driven primarily by a 42.5% rise in minimum CSA; maximum CSA remained essentially unchanged (+0.3%, $p = 0.91$) (Table 2; Fig. 3). Maximum CSA therefore declined in ASTRO 0, ASTRO 2 and ASTRO 3 but not in ASTRO 1.

Pulsatile excursion (PE), expressed as the coefficient of variation of IJV-CSA within the cardiac cycle (standard deviation divided by the mean), increased significantly from pre-flight to post-flight 1 in ASTRO 2 (+337.1%, $p < 0.001$) and ASTRO 0 (+105.0%, $p < 0.001$); the increase of 24.5% in ASTRO 3 showed the same trend but did not reach significance ($p = 0.08$). In ASTRO 1, PE decreased by 60.3% ($p < 0.001$) (Table 2). The only in-flight pulsatility data are those of ASTRO 0.

At the second post-flight session of ASTRO 1, B-mode ultrasound showed clear thrombi within both valve pockets of the right IJV. The relationship between this finding and the reduced venous collapsibility recorded at post-flight 1 is considered in the Discussion.

Heart rate was derived for every astronaut and every session from the RR intervals of the electrocardiographic channel recorded simultaneously with the ultrasound acquisition and is reported in Table 2.

Table 1 Characteristics of the cohort under study.

Characteristic	Value
Astronauts studied	4 (ASTRO 0, ASTRO 1, ASTRO 2, ASTRO 3)
Sex ratio	1:1
Age at launch, years, mean (SD)	44.75 (7.95)
Mission duration, days, mean (SD)	166 (21)
Pre-flight session, days before launch	30 in all astronauts
In-flight session 1, days after docking	ASTRO 0 only, 5
In-flight session 2, days after docking	ASTRO 0 only, 156
Post-flight 1, days after splashdown, mean (SD)	6 (1)
Post-flight 2, days after splashdown, mean (SD)	32 (3)
Side examined	Right internal jugular vein in all astronauts
Body position, ground sessions	Supine
Body position, in-flight sessions	Neutral body position, free floating
Breathing	Spontaneous, not controlled

Individual demographic and anthropometric data cannot be disclosed, since the crew members are identifiable within a very small population and the confidentiality provisions of the agreements between the Italian Space Agency and NASA prohibit the release of individual-level data.

Table 2 Longitudinal changes in internal jugular vein cross-sectional area (IJV-CSA), in pulsatile excursion (PE) and in heart rate.

	ASTRO 1	ASTRO 2	ASTRO 3	ASTRO 0
Mean IJV-CSA, cm^2				
Pre-flight, mean (SD)	1.041 (0.096)	1.083 (0.021)	1.460 (0.066)	0.723 (0.076)
Post-flight 1, mean (SD)	1.243 (0.059)	0.584 (0.093)	0.754 (0.089)	0.453 (0.061)
Post-flight 2, mean (SD)	1.732 (0.028)	1.206 (0.062)	1.379 (0.093)	0.466 (0.039)
Change (%), Pre-flight vs Post-flight 1 / p value	+19.3% / p<0.0001	−46.0% / p<0.0001	−48.4% / p<0.0001	−37.9% / p<0.0001
Change (%), Pre-flight vs Post-flight 2 / p value	+66.4% / p<0.0001	+11.4% / p<0.0001	−5.5% / p=0.01	−36.2% / p<0.0001
Minimum IJV-CSA, cm^2				
Pre-flight, mean (SD)	0.785 (0.148)	1.029 (0.030)	1.293 (0.077)	0.699 (0.069)
Post-flight 1, mean (SD)	1.119 (0.077)	0.449 (0.103)	0.630 (0.102)	0.401 (0.055)
Post-flight 2, mean (SD)	1.684 (0.040)	1.077 (0.050)	1.281 (0.098)	0.4417 (0.044)
Change (%), Pre-flight vs Post-flight 1 / p value	+42.5% / p<0.0001	−56.4% / p<0.0001	−51.3% / p<0.0001	−42.7% / p<0.0001
Change (%), Pre-flight vs Post-flight 2 / p value	+114.5% / p<0.0001	+4.7% / p=0.01	−0.9% / p=0.75 (n.s.)	−36.8% / p<0.0001
Maximum IJV-CSA, cm^2				
Pre-flight, mean (SD)	1.336 (0.108)	1.143 (0.0197)	1.770 (0.088)	0.762 (0.076)
Post-flight 1, mean (SD)	1.341 (0.063)	0.714 (0.0883)	0.968 (0.072)	0.487 (0.069)
Post-flight 2, mean (SD)	1.763 (0.0201)	1.328 (0.0753)	1.455 (0.098)	0.489 (0.050)
Change (%), Pre-flight vs Post-flight 1 / p value	+0.3% / p=0.91 (n.s.)	−37.5% / p<0.0001	−45.3% / p<0.0001	−36.0% / p<0.0001
Change (%), Pre-flight vs Post-flight 2 / p value	+31.9% / p<0.0001	+16.2% / p<0.0001	−17.8% / p<0.0001	−35.8% / p<0.0001
Pulsatile Excursion (PE), coefficient of variation				
Pre-flight, CV±SD	0.174±0.066	0.035±0.009	0.105±0.023	0.032±0.012
Post-flight 1, CV±SD	0.069±0.013	0.153±0.050	0.131±0.034	0.065±0.025
Post-flight 2, CV±SD	0.014±0.006	0.070±0.015	0.043±0.014	0.032±0.013
Change (%), Pre-flight vs Post-flight 1 / p value	−60.3% / p<0.001	+337.1% / p<0.0001	+24.5% / p=0.08 (n.s.)	+105.0% / p<0.0001
Change (%), Pre-flight vs Post-flight 2 / p value	−92.0% / p<0.0001	+101.3% / p<0.0001	−59.6% / p<0.0001	−0.4% / p=0.96 (n.s.)
Heart Rate (HR), beats per minute (BPM)				
Pre-flight, BPM	69	66	60	60
Post-flight 1, BPM	92	76	57	78
Post-flight 2, BPM	75	64	66	56

Abbreviations. IJV-CSA, internal jugular vein cross-sectional area; Min-CSA, minimum CSA per cardiac cycle, corresponding to the x-descent of the jugular venous pulse; Max-CSA, maximum CSA per cardiac cycle, corresponding to the a-wave; PE, pulsatile excursion, that is the coefficient of variation, standard deviation divided by mean; HR, heart rate; BPM, beats per minute. Pre-flight, 30 days before launch. In-flight 1 and in-flight 2, approximately one week and five months after docking, ASTRO 0 only. Post-flight 1, within one week of splashdown. Post-flight 2, approximately 30 days after splashdown. The unit of analysis is the cardiac cycle within subject; p values derive from two-tailed Student t tests for independent samples, comparing each post-flight session with the pre-flight session of the same astronaut.

Discussion

This study shows that the JVP is detectable and can be quantified non-invasively before and after long-duration spaceflight and, in one astronaut, in microgravity itself. The JVP waveform preserved its expected morphology and temporal relationship to the simultaneously recorded electrocardiogram: the maximum area occurred in the interval corresponding to the a-wave and the minimum area in the interval corresponding to the x-descent (Fig. 1). The correspondence between these features and right atrial pressure rests on our previous ground-based validation against invasive measurement[9]; no equivalent validation was possible in microgravity.

The IJV-CSA values observed here are smaller than those reported in previous spaceflight studies[7,8]. The comparison is meaningful only when the posture of the reference measurement is stated. Our pre-flight measurements were acquired in the supine position, which produces the largest IJV-CSA on Earth[5,6,12], and ranged in this study from 0.723 to 1.460 cm^2. Earlier investigations acquired their pre-flight reference in the seated position, which produces the smallest area because of the negative transmural pressure, and compared it with data acquired in microgravity; the transition to weightlessness therefore necessarily appeared as a marked increase in CSA. In our series the post-flight 1 values (0.453–1.243 cm^2) and the in-flight values of ASTRO 0 lie below a supine

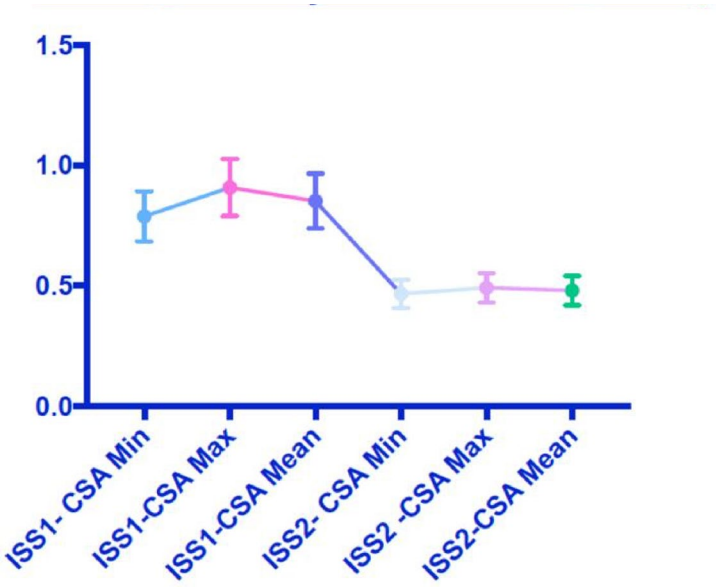


Fig. 2 ASTRO 0 in-flight IJV-CSA longitudinal changes. JVP parameters assessed from self-performed B-mode video clips in two in-flight sessions, respectively five days and five months after ISS docking. Significant changes in the mean, minimum and maximum IJV-CSA are apparent at five months. These data derive from a single astronaut. Cited in the Results and in the Discussion.

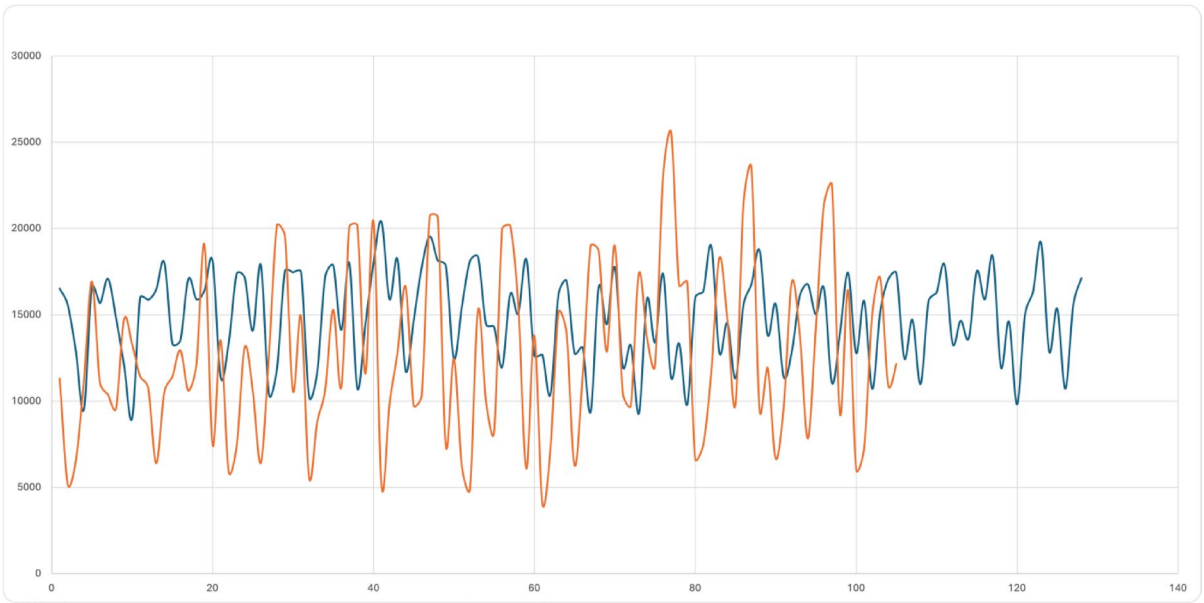


Fig. 3 Representative jugular venous pulse waveforms derived from B-mode ultrasound of the IJV. Cross-sectional area recorded at pre-flight (orange signal) and at post-flight 1 (blue signal) in ASTRO 1. The significant increase in the minimum CSA after flight, compared with pre-flight, is clearly represented, together with the corresponding reduction in pulsatile excursion. Cited in the Results and in the Discussion.

terrestrial reference rather than above a seated one. The direction of the reported change is therefore governed by the reference posture adopted on Earth rather than by a difference in the response to microgravity exposure.

Transmural pressure is not the sole determinant of the postural difference in IJV-CSA. Venous compliance and wall tone, respiratory modulation of intrathoracic pressure, cervical muscle tone, probe pressure, plasma volume status and the difference between single-frame and multi-frame analysis all contribute [4–6,12]. Two methodological points further affect the comparison. First, prior spaceflight studies relied on single-frame images, whereas we analysed 15–20 frames per cardiac cycle, permitting determination of the mean, minimum and maximum CSA and of the pulsatile excursion rather than of a single value of uncertain phase (Table 2; Figs. 3, 4). Second,

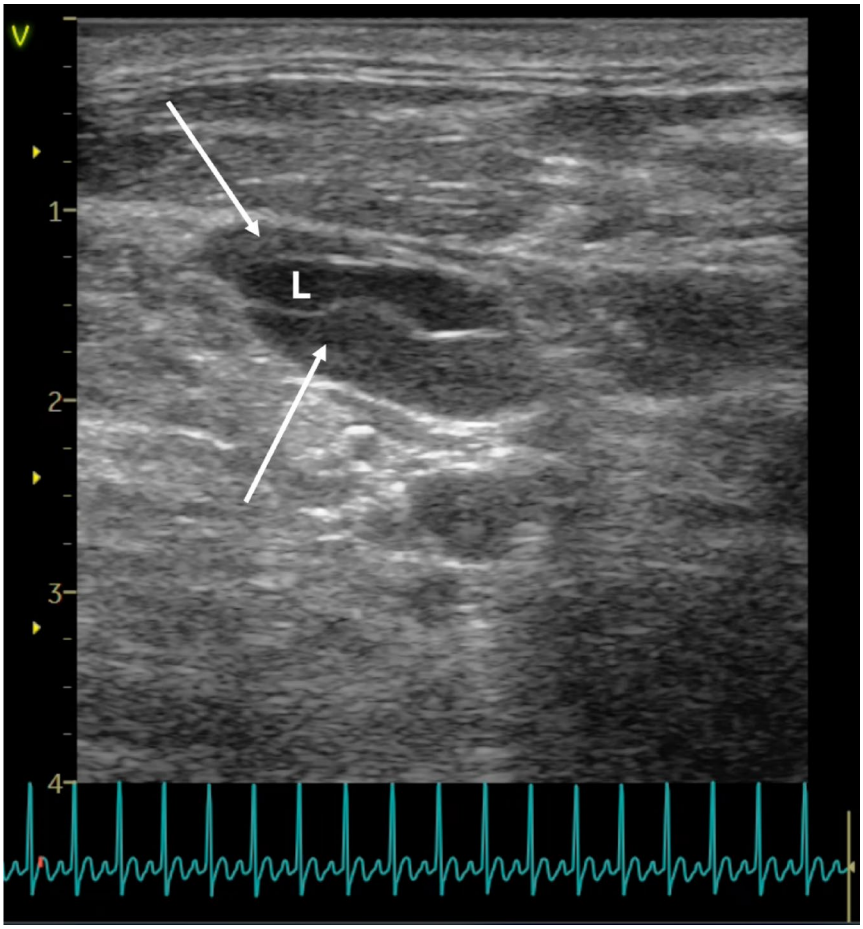


Fig. 4 B-mode frame of the right internal jugular vein time-aligned with the simultaneously recorded electrocardiographic trace. Right internal jugular vein at the J1 segment in ASTRO 1, in the first post flight data collection. The red vertical marker indicates the position of the displayed frame within the cardiac cycle, so that the correspondence between the maximum cross-sectional area and the a-wave interval, and between the minimum cross-sectional area and the x-descent interval, can be verified directly. Cited in the Methods and in the Discussion. On the left calibrated depth scale graduated in centimetres. Legend: L = anechoic lumen; arrows indicate the two valve pockets with organized clotting material inside.

breathing was not controlled, so respiratory variation is embedded in our measurements. Seated and semi-recumbent acquisitions were not obtained, and we therefore cannot locate our in-flight and post-flight values between the two postural extremes within the same individuals.

The longitudinal description derives from a single astronaut (ASTRO 0). In this participant mean IJV-CSA was essentially unchanged within the first week in orbit and significantly reduced at five months; the reduction persisted into the early post-flight period and was still present one month after return (Table 2). Maximum CSA, which corresponds to the a-wave and correlates with central venous pressure[9], declined over the same interval in ASTRO 0, ASTRO 2 and ASTRO 3, consistent with reduced preload.

We do not have concurrent plasma volume or haematocrit determinations, but plasma volume contraction is known to occur within the first days to weeks of microgravity exposure and then stabilise[13,14], so that it cannot by itself account for a reduction in venous calibre becoming apparent only at five months. We propose a multifactorial explanation that respects this time course: an early hypovolaemic component that stabilises and thereafter contributes a constant offset; a sustained reduction in central venous pressure and venous filling throughout the mission; progressive loss of red-cell mass, which follows a slower time course than the plasma compartment and persists over months[15]; and structural remodelling of the cerebral venous compartment together with changes in venous compliance described after long-duration flight[16]. In the absence of volume, haematological and vessel-wall data acquired in the same subjects, this account remains a hypothesis and a specific target for future missions.

Pulsatile excursion increased from pre-flight to the early post-flight session in three of the four astronauts (highly significantly in ASTRO 2 and ASTRO 0, with a trend in ASTRO 3). To our knowledge an increased transmission of cardiac pressure waves towards the brain in association with spaceflight has not been described previously; the reason appears methodological rather than biological. Pulsatile excursion cannot be computed

from the single-frame or single-phase acquisitions used in previous spaceflight studies[7,8]. The increase in the pulsatile excursion of the IJV corresponds to increased retrograde propagation of cardiac pressure waves along the vein. In the absence of the hydrostatic gradient this propagation is expected to reach the cerebral venous compartment less attenuated. It has been proposed that increased pulsatility within the perivenous compartment influences the resorption of cerebrospinal fluid along the perivenous spaces[17,18], and that impaired glymphatic clearance contributes to the ocular manifestations of spaceflight-associated neuro-ocular syndrome [19–21]. Both the latter very well-known microgravitational pathophysiological manifestations might have a contribution by our findings of increased pulsatility transmitted upward the peri-venous space. However, such a hypothesis merits further investigations by the mean of serial waveform analysis to be combined, within the same crew members, with optical coherence tomography, surrogates of intraocular and intracranial pressure, and neuroimaging measures of glymphatic function.

Moreover, in ASTRO 1 an opposite pattern was observed: markedly increased minimum CSA and reduced pulsatile excursion at both post-flight sessions (Table 2; Fig. 3). B-mode ultrasound performed 21 days after splashdown revealed a clear B-mode image of clots within both valve pockets of the right IJV (Fig. 4). We consider that the thrombi were already present and wall-adherent at post-flight 1, where it altered the mechanics of the segment without being clearly visible at the conventional B-mode imaging. In its early phase the venous clots are close to isoechoic with circulating blood, so grey-scale imaging might fail to distinguish material lodged between the valve leaflet and the wall from luminal blood. On this reading the alteration of the JVP parameters in ASTRO 1 is a consequence of the thrombus rather than a cause of it. The absence of any examination between post-flight 1 and post-flight 2 is the main reason the thrombi were definitely detected only at 21 days.

The finding rests on high-resolution B-mode ultrasound reviewed independently by experienced operators; the appearance is characteristic. Confirmatory modalities (dedicated Angio MRI/CT, laboratory markers of thrombosis) were not part of the approved protocol and are not available; post-flight clinical management fell under the responsibility of the flight surgeons.

This constrains the strength of any conclusion drawn from this single case, which is, to our knowledge, the third jugular thrombosis reported in space medicine to date[7,8], no further case having been detected in the eleven astronauts examined bilaterally in the NASA occupational surveillance programme[21].

This study has several limitations. The sample comprises four astronauts, and in-flight acquisitions were obtained in only one of them; the longitudinal in-flight series therefore rests on a single participant and no population-level inference is possible. The unit of analysis is the cardiac cycle within subject; the reported p values quantify within-subject variability across cycles rather than variability between astronauts. Only the right IJV was examined; side-to-side differences are substantial in the general population, so our findings describe the right side and cannot be extrapolated to global cerebral venous outflow. Breathing was not controlled, and respiratory variation therefore contributes to the variability of the area parameters, particularly of the pulsatile excursion, although every clip spanned more than one complete respiratory cycle. Ground-based acquisitions were performed by a trained operator, whereas the in-flight acquisitions were necessarily self-performed, introducing an unavoidable operator difference between phases. No plasma volume, haematocrit, echocardiographic or venous Doppler data were available to us, because these assessments are performed by the flight surgeons under separate medical protocols outside the data-sharing scope of the contract governing this study; multi-modality imaging was not part of the approved Drain Brain 2.0 protocol at all time points. Right atrial pressure was not measured, so the physiological interpretation of the waveform in microgravity rests on our previous terrestrial validation. Finally, individual demographic and anthropometric data cannot be disclosed for the confidentiality reasons stated in the Methods, so only demographic aggregate values are reported in Table 1. These constraints reflect the logistical and regulatory difficulties of space research and may be addressed in future missions with larger crews and a broader approved protocol.

Ultrasound assessment of the JVP, performed with portable equipment synchronised with the electrocardiogram, proved feasible for self-acquisition in orbit after targeted training. Combined with automated segmentation it yields waveform parameters that cannot be obtained from single-frame acquisition. Whether these parameters

carry predictive value for jugular venous thrombosis is an open question that the present series can raise but not answer. The appropriate next step is a ground-based validation study in patients with established IJV thrombosis and in patients at elevated risk, in which the diagnostic performance of the area and pulsatility parameters could be quantified in a sample of adequate size. Only if such a study established their discriminative value would their use as a monitoring tool during long-duration missions be justified.

Methods

Study design and participants

This study was conducted within the framework of the Drain Brain projects sponsored by the Italian Space Agency (ASI). Four astronauts (ASTRO 0, ASTRO 1, ASTRO 2 and ASTRO 3) were enrolled. All participants provided written informed consent. The study protocol was approved by the Comitato Etico di Area Vasta Emilia Centro (CE AVEC) and by the NASA Institutional Review Board and was performed in accordance with the Declaration of Helsinki.

All four astronauts were examined pre-flight on Earth and at two post-flight sessions. In-flight acquisitions were obtained in ASTRO 0 only, at two time points corresponding to approximately one and five months after docking; the other astronauts data acquisition timeline are given in Table 1.

The crew members are identifiable within a very small population, and the confidentiality provisions of the agreements between the Italian Space Agency and NASA prohibit the release of individual-level demographic and anthropometric data. We therefore report aggregate values only, given in Table 1. This restriction is regulatory in nature and is not an omission on our part.

Ultrasound image acquisition

High-resolution B-mode ultrasound video-clips of the right IJV were acquired in the transverse plane at the level of the J1-J2 segment, immediately cranial to the valve apparatus. The same portable ultrasound system was used for all acquisitions, both at the Johnson Space Center (Houston, Texas) and aboard the ISS, so that imaging parameters and probe characteristics were identical across all experimental phases.

The system was a (Vivid-Q scanner, GE Medical Systems Ultrasound, Horten, Norway) equipped with a high-resolution linear-array probe operating between 7 and 12 MHz. Clips were recorded at a frame rate of at least 15 Hz and each lasted between 10 and 15 s, so that every acquisition spanned about 3 complete respiratory cycle. A simultaneous three-lead electrocardiographic trace was recorded and synchronised with the ultrasound video to align the IJV-CSA changes with the cardiac cycle. Figure 4 shows a representative frame time-aligned with the corresponding electrocardiographic trace. For each session, 15 to 20 frames per cardiac cycle were analysed, covering complete heartbeats.

Only the right IJV was examined, for four reasons. The right vein is the dominant cerebral venous outflow route in most individuals and drains into the right atrium along a shorter and straighter course, so that the transmitted pressure wave reaches it less attenuated. It is the side conventionally used for the clinical assessment of the JVP on Earth and for central venous access. The choice preserves comparability with the acquisition protocol of the previous Drain Brain study[10]. Finally, the operational time available to a crew member performing a self-acquisition in orbit does not permit a bilateral examination. We recognise that side-to-side differences are substantial in the general population; the consequences of this choice for the interpretation of our findings are stated in the Limitations.

On Earth, acquisitions were performed with the subject in the supine position; seated or semi-recumbent acquisitions were not obtained. In microgravity, ASTRO 0 performed self-acquired scans in the neutral body position (the crew member floated freely with the trunk unsupported, the arms relaxed and the neck in a comfortable

posture, neither flexed nor extended, approximating the natural resting posture of the cervical spine in weightlessness). No foot restraints were used. In the absence of a positioning device this is the only configuration operationally available in orbit. Breathing was not actively controlled; all subjects breathed spontaneously, both on Earth and in orbit, and neither a Valsalva manoeuvre nor breath-holding was performed. Spontaneous respiration was adopted deliberately to reflect real operational conditions and to avoid the confounding effects of forced apnoea or paced breathing on venous return. Since every clip spanned more than one respiratory cycle, the per-session averages incorporate rather than exclude the respiratory variation; the consequences of this are addressed in the Limitations.

All ground-based acquisitions (pre-flight and post-flight) were performed by the same trained operator; the acquisitions in ASTRO 1, ASTRO 2 and ASTRO 3 were performed by the same operator, with the aim of minimising inter-operator variability in the within-subject comparisons. ASTRO 0 acquired repeated in-flight measurements at two time points during the mission; these acquisitions were necessarily self-performed after a dedicated and previously validated training programme[10]. This case confirms the technical feasibility of reliable self-performed JVP assessment in orbit by a non-physician astronaut, and at the same time introduces an operator difference between the in-flight and the ground-based sessions that cannot be avoided in this setting and is stated in the Limitations.

Image processing and JVP waveform derivation

Ultrasound videos were analysed offline. IJV contours were segmented semi-automatically with the support of a previously validated artificial intelligence model based on a U-Net convolutional neural network[22]. The model achieved a median Dice coefficient of approximately 0.91 versus expert annotations, with an HD95 of 8–10 pixels, demonstrating excellent agreement with human raters (ICC = 0.94) and non-inferiority to manual segmentation. Manual segmentation of the 3855 frames analysed here would not be compatible with an operational timeline and carries an inter-observer variability of a magnitude comparable with the effects under investigation, which is the reason for the automated approach. CSA was measured frame by frame and converted to cm^2 using the calibration embedded in the ultrasound system. For each cardiac cycle the following parameters were derived: mean CSA; minimum CSA (corresponding to the x-descent of the JVP); maximum CSA (corresponding to the a-wave of the JVP); and pulsatile excursion (PE), calculated as the coefficient of variation (standard deviation divided by the mean CSA within the cycle).

The JVP waveform was reconstructed by plotting the CSA variations over time synchronised with the electrocardiographic trace. Heart rate was derived for every session from the RR intervals of the same electrocardiographic channel and is reported in Table 2. All segmentations underwent quality control by experienced operators.

Statistical analysis

The present study was not designed as a sampling-based population study. The research question was addressed within each participant, namely whether the parameters measured at a given post-flight session differ from the pre-flight baseline of that same astronaut, and each astronaut was therefore analysed separately as an individual longitudinal series.

The unit of analysis is the cardiac cycle within subject. Continuous variables are expressed as mean ± standard deviation. For every astronaut and every parameter, two comparisons were performed, pre-flight against post-flight 1 and pre-flight against post-flight 2, using the two-tailed Student t test for independent samples on the per-cycle values of the two sessions concerned. Percentage changes were calculated as ((post-flight value − pre-flight value) / pre-flight value) × 100. A p value below 0.05 was considered statistically significant. Analyses were performed with GraphPad Prism and R.

Both comparisons were specified in advance, and both refer to a common baseline, and an omnibus analysis of variance across the three sessions was therefore not performed. Its null hypothesis, that the means of the three

sessions are equal, does not correspond to the question posed, the sessions being ordered states of adaptation rather than exchangeable levels of a factor, and the acceptance or rejection of that intermediate hypothesis would not modify the two contrasts that carry the physiological meaning.

Because the unit of analysis is the cardiac cycle within subject, the p values reported quantify within-subject variability across cardiac cycles and not variability between astronauts, and no inference beyond the individual participant is intended.

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Author contributions PZ: study conception and design, data interpretation, draft critical revision, final approval APa: data collection, data processing, drafting, final approval AB: data extraction and analysis, final approval GF: data collection and drafting, final approval APr: data extraction and analysis, final approval MZ: critical revision, blinded quality control, final approval RB: data extraction and analysis, final approval AT: project manager, organization of the experimental sessions, final approval All authors approved the final draft and had access to data.

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Data availability The raw ultrasound clips cannot be released, since they constitute crew medical data governed by the confidentiality provisions of the agreements between the Italian Space Agency and NASA. Requests concerning the raw imaging material should be addressed to the corresponding author and are subject to the authorisation of the agencies concerned.

Code availability The convolutional segmentation pipeline based on the U-Net architecture, the routines for the per-cycle extraction of the area parameters and the statistical analysis scripts have been deposited in Zenodo under DOI (https://doi.org/10.5281/zenodo.21776027), with the version tag corresponding to the analyses reported in this manuscript. The same record contains the derived per-frame dataset, so that the analyses may be reproduced in full of the deposited material. The repository is also cited in the Methods.

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