J. M. Dickson[1]
H. M. Weavers[2]
N. Mitchell[2]
E. M. Winter[2]
I. D. Wilkinson[3]
E. J. R. Van Beek[3]
J. M. Wild[3]
P. D. Griffiths[3]

The Effects of Dehydration on Brain Volume – Preliminary Results

Abstract

In adults the cranium is a rigid bony vault of fixed size and therefore the intra-cranial volume is a constant which equals the sum of the volume of the brain, the intra-cranial volume of CSF and the intra-cranial volume of blood. There can be marked changes in the volumes of these three intra-cranial compartments which may influence susceptibility to brain damage after head injury. This is the first study to investigate the relationship between dehydration and changes in the volume of the brain and the cerebral ventricles. Six healthy control subjects underwent magnetic resonance imaging of the brain before and after a period of exercise in an environmental chamber. The subjects lost between 2.1% and 2.6% of their body mass due to water loss through sweating. We found a correlation between the degree of dehydration and the change in ventricular volume ($r = 0.932$, $p = 0.007$). The changes in ventricular volume caused by dehydration were much larger than those seen in day-to-day fluctuations in a normally hydrated healthy control subject.

Key words
Dehydration · head injury · brain volume · ventricular volume · sports injuries · stereology

Introduction

The brain and spine are completely enveloped by three layers of tissue known as the meninges. The toughest and most superficial is the dura mater, next is the arachnoid mater, and on the surface of the brain is the pia mater. One role of the meninges is to protect the brain by fixing its position, thereby limiting collisions with the skull. In addition, the arachnoid mater contains a pool of cerebrospinal fluid (CSF) in a compartment known as the sub-arachnoid space. The brain is suspended within the sub-arachnoid space which reduces the effective weight of the brain and surrounds it with a protective cushion of fluid.

The brain contains fluid filled cavities known as the cerebral ventricles which communicate with the subarachnoid space via three small foramen around the fourth ventricle. Within the ventricles is an extended structure called the choroid plexus which secretes CSF at a rate of about 450 ml per day [1]. The ventricles themselves have a volume of approximately 25 ml [2] and so their CSF content is completely renewed about eighteen times per day. CSF drains from the ventricles through the foramina of the fourth ventricle where it enters the subarachnoid space. Within this compartment – which contains about 125 ml of CSF – CSF flows upwards towards the apex of the cranium where it flows through specialised structures known as arachnoid villi.

Affiliation
[1] Department of Biomedical Science, The University of Sheffield, Sheffield, UK
[2] Centre for Sport and Exercise Science, Sheffield Hallam University, Sheffield, UK
[3] Unit of Academic Radiology, The University of Sheffield, Sheffield, UK

Correspondence
J. M. Dickson · Magdalen College, The University of Oxford · OX1 4 AU · Oxford · United Kingdom · Phone: + 07793234223 · Fax: + 01865276030 · E-mail: jon.dickson@magdalen.oxford.ac.uk

Accepted after revision: June 30, 2004

Bibliography
Int J Sports Med 2005; 26: 481 – 485 © Georg Thieme Verlag KG · Stuttgart · New York · DOI 10.1055/s-2004-821318 · Published online September 27, 2004 · ISSN 0172-4622

The arachnoid villi project into the dural venous sinuses and from here CSF flows into the external jugular vein and enters the systemic circulation.

The cranium is a rigid bony vault of fixed size. The Monro-Kellie hypothesis [3] states that the sum of the volumes of the brain, the intra-cranial CSF, and the intra-cranial blood are a constant which is equal to the intra-cranial volume. Exercise induced dehydration can cause a decrease in blood volume (hypovolaemia) which may change intra-cerebral blood volume. Dehydration can also increase plasma osmolarity which may cause changes in brain volume [4] due to osmotic changes in neuronal volume. Both effects will result in compensatory changes in intra-cranial CSF volume which may occur in the ventricles, the subarachnoid space, or both. Changes in intra-cranial volumes which exceed the capacity of the choroid plexus to replace the lost volume with CSF cause CSF to be drawn into the cranium from the dural sac of the spinal cord [5]. Unlike the dura of the brain, the spinal dura is not encased in bone and can contract and expand in response to changes in intra-cranial pressure. CSF production by the choroid plexus eventually corrects the shortfall and the spinal dura assumes its normal volume.

The relationship between dehydration and the volume of the brain, the intra-cranial blood, and the intra-cranial CSF is likely to be complex. As far as we are aware there have been no previous studies in humans that have investigated the effects of exercise induced dehydration on the volumes of the intra-cranial compartments. Changes in the volume of the brain, the intra-cranial CSF (especially the subarachnoid space), and the intra-cranial blood may influence the outcome of closed head injuries. After an impact to the head the brain will travel further within the cranium before it meets the skull if the subarachnoid space is enlarged than in the normally hydrated state. Consequently it will accelerate to higher velocities and this may increase the likelihood of contusion injuries after blows to the head such as those sustained in boxing, football, and rugby [6]. Enlargement of the subarachnoid space also makes the veins which span this compartment more vulnerable to rupture in head injury [7].

In summary, dehydration may significantly increase the risk of brain damage after a head injury by changing the volumes of the intra-cranial compartments. Therefore we designed a study to investigate the effects of exercise-induced dehydration on the volume of the brain and the cerebral ventricles in a small group of amateur rugby union players.

Material and Methods

Dehydration and scanning

Six subjects took part in the study which was approved by the School of Sport and Leisure Management Research Ethics Committee of Sheffield Hallam University. All the subjects gave informed consent. They were male amateur rugby union players between the ages of 18 and 25 (mean age = 19.8) who trained regularly. The subjects underwent magnetic resonance imaging (MRI) before and after a period of exercise designed to cause significant dehydration. In addition, samples of blood and urine were taken before and after the exercise to assess the degree of dehydration.

The schedule began at approximately 9 am with the pre-dehydration MRI scan. MR was performed at 1.5 T (Eclipse, Philips Medical Systems, Cleveland, Ohio) in the Unit of Academic Radiology. T_1-weighted volumetric data sets were acquired using a 3-dimensional radiofrequency-spoiled gradient-recalled echo fast acquisition in the steady-state (RF-FAST) technique. The second phase-encoded direction lay along the anterior-posterior line. Data were acquired using a standard receive-only quadrature head coil. The sequence and its associated parameters (TR = 15 ms; TE = 4.4 ms; slice thickness 1 mm) were chosen to yield a T_1-weighted data set with an isotropic spatial resolution of 1 mm^3 over the entire cranium. The procedure took about 20 minutes.

Once complete the subject was taken to the Centre of Sport and Exercise Science where body fat percentage was calculated using bioelectrical impedance and height and body mass were measured. Blood samples were taken by venepuncture. The blood was centrifuged and the serum was analysed for concentrations of K^+, Na^+, urea, and creatine. In addition, finger prick samples were taken in triplicate and analysed for haemoglobin and haematocrit concentrations. Urine samples were also taken in triplicate and analysed for osmolality. Finally, core body temperature was assessed by tympanic thermometry.

The subject was taken to an environmental chamber, where he exercised for approximately one hour at 31 °C (± 1°) and 40% (± 2%) humidity. Dehydration was assessed by percentage loss of body mass and the target was 2.5%. The exercise was interrupted every twenty minutes when body mass was measured and dehydration assessed. Throughout the exercise period heart rate and core body temperature were measured to ensure the subject's safety. Once complete the subject was allowed to rest for approximately one hour after which body mass was measured, blood and urine samples were taken, and the subject was returned to the Unit of Academic Radiology for the post-dehydration scan.

Volumetric analysis

Post-acquisition volumetric analyses were performed off-line on coronal sections of the 3-dimensional dataset within the biomedical imaging package Analyze™ version 7.0 (Mayo Clinic, MN, USA) [8]. The scans were analysed volumetrically on a SPARC 20 workstation (SUN Microsystems, CA, USA). Volumetric analysis was performed using the stereology programme of Analyze™ using the point counting technique. The volume of the brain and the cerebral ventricles was measured using a cross size of 3 × 3 voxels and a slice increment of 5. The same cross size was used to measure the brain and the ventricles.

The person measuring the volumes (HMW) was blind to the identity of the scans which were labelled using an alpha-numeric code. Six of the scans from the dehydration series were measured twice by HMW. This allowed calculation of an intra-class correlation coefficient (ICC) which is used as an indication of intra-rater reliability. An ICC of 1 indicates perfect repeatabil-

Table **1** Personal statistics and pre- and post-dehydration values for blood and urine assessments

	Sub 1		*Sub 2*		*Sub 3*		*Sub 4*		*Sub 5*		*Sub 6*	
	Pre	*Post*	*Pre*	*Post*	*Pre*	*Post*	*Pre*	*Post*	*Pre*	*Post*	*Pre*	*Post*
Height (cm)	192.8	–	174.0	–	195.0	–	175.3	–	183.0	–	179.0	–
Body fat (%)	21.2	–	13.9	–	10.6	–	19.9	–	18.9	–	23.4	–
Body mass (kg)	107.5	105.3	68.6	66.3	79.6	76.8	85.9	84.2	89.3	86.6	93.4	91.8
Serum sodium ($mmol \cdot l^{-1}$)	132.18	132.18	128.55	135.86	135.86	132.18	135.86	200.78	128.55	135.86	135.86	200.78
Serum potassium ($mmol \cdot l^{-1}$)	4.16	4.28	3.92	4.36	4.27	4.22	3.93	4.42	4.07	4.30	4.50	5.37
Serum urea ($mmol \cdot l^{-1}$)	5.61	5.65	5.90	5.84	6.23	6.82	7.20	7.63	6.82	6.57	4.74	6.12
Serum creatinine ($\mu mol \cdot l^{-1}$)	69.3	81.6	68.3	76.4	73.1	76.8	68.3	83.2	75.6	108	70.9	85.9
Serum haemoglobin (g/dl)	15.8	17.3	14.2	16.2	16.8	17.2	13.9	14.4	13.3	15.4	16.2	16.9
Serum haematocrit (%)	45	46	44	47	45	46	43	48	43	45	45	46
Serum osmolality ($mmol \cdot l^{-1}$)	297	306	296	304	290	296	293	301	293	309	295	310
Urine osmolality ($mmol \cdot l^{-1}$)	342	804	338	429	64	451	188	497	150	428	328	466

ity and 0 indicates randomness. We also calculated the test-retest coefficient of variation.

Results were analysed using SPSS version 10 (SPSS Inc, Chicago, USA) for windows. Paired *t*-tests were used to compare means and the Pearson product moment correlation coefficient was used to investigate the relationship between variables. Statistical significance was taken to be at $p \leq 0.05$.

Normally hydrated subject

Subject 4 undertook a further series of MRI scans so we could assess day-to-day fluctuations of brain and ventricular volume in a normally hydrated healthy control subject. He was scanned at approximately 9 am (range 8.15 am – 9.30 am) on four consecutive days. During this period he was asked to abstain from alcohol and not to undertake any significant exercise. The scans were acquired and analysed using the same method as described above.

Results

Blood and urine

The mean decrease in body mass of the subjects due to dehydration was 2.31 % (SD = 0.19). Table **1** shows the pre- and post-dehydration values of the blood and urine measures. There was a statistically significant difference between pre- and post-dehydration values for serum potassium concentration ($t[df] = -2.645(5)$, $p = 0.046$), serum creatine concentration ($t[df] = -3.588(5)$, $p = 0.016$), blood haemoglobin concentration ($t[df] = -3.846(5)$, $p = 0.012$), blood haematocrit concentration ($t[df] = -3.313(5)$, $p = 0.021$), serum osmolality ($t[df] = -6.127(5)$, $p = 0.002$), plasma volume ($t[df] = 5.648(5)$, $p = 0.002$), and urine osmolality ($t[df] = -4.776(5)$, $p = 0.005$). There was no statistically significant difference between the pre- and post-dehydration values for serum sodium concentration ($t[df] = -1.774(5)$, $p = 0.136$) and serum urea concentration ($t[df] = -1.470(5)$, $p = 0.201$).

Table **2** Volume of the brain and cerebral ventricles of each subject pre- and post-dehydration

		Ventricles		*Brain*	
Subject	*Dehydration (%)*	*Pre (mm^3)*	*Post (mm^3)*	*Pre (mm^3)*	*Post (mm^3)*
1	2.30	19730	20375	1027984	1011641
2	2.50	17956	19837	1074754	1106418
3	2.60	18278	24783	1011970	1006534
4	2.24	13655	14461	983740	1026586
5	2.14	21127	19353	936432	997126
6	2.10	31825	27632	989062	839343

Volumetric analysis

The ICC was 0.99 and the test-retest coefficient of variation was 6.6 % which indicates excellent measurement repeatability. Table **2** shows the volume of the brain and the cerebral ventricles of each subject pre- and post-dehydration. There was no significant difference between the mean pre- and post-dehydration values

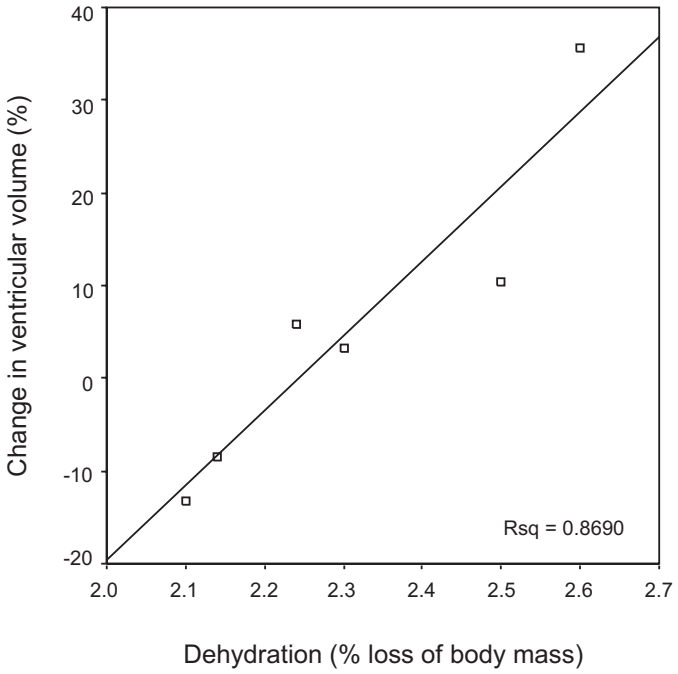

Fig. **1** The relationship between dehydration and change in ventricular volume.

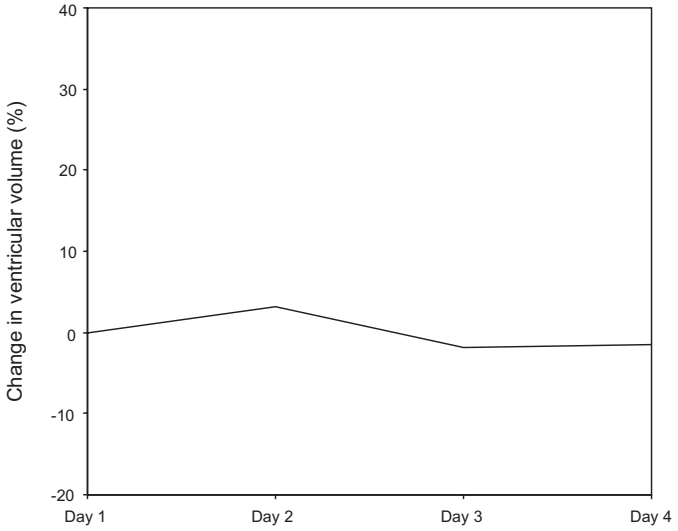

Fig. **2** Change in ventricular volume over four days whilst the subject was normally hydrated.

for brain volume ($t[df] = 0.195(5)$, $p = 0.853$) and ventricular volume ($t[df] = -0.438(5)$, $p = 0.680$).

There was a correlation between dehydration (i.e., percentage change in body mass due to exercise) and percentage change in ventricular volume ($r = 0.932$, $p = 0.007$). This correlation is shown in Fig. **1**. There was no correlation between dehydration and percentage change in brain volume ($r = 0.286$; $p = 0.583$).

Normally hydrated subject

The change in ventricular volume over the four days is shown graphically in Fig. **2**. The mean ventricular volume over the four days was 13 929 mm^3 and the mean magnitude (i.e., size of change regardless of direction) of deviation from this value on each of the four days was 1.63% (range 0.10 – 3.09%).

Discussion

As far as we are aware this is the first study to investigate the relationship between dehydration and the volume of the brain and cerebral ventricles in humans. We have shown a correlation between dehydration and ventricular volume which is of a much larger magnitude than day-to-day fluctuations observed in a normally hydrated healthy control subject.

The correlation between dehydration and change in ventricular volume is peculiar. At low levels of dehydration (up to approximately 2.2% loss of body mass) ventricular volume decreases but when dehydration becomes more severe ventricular volume increases. Since there are no correlations between any of the physiological markers of dehydration (i.e., concentrations of blood and urine contents) and the change in ventricular volume the cause of this effect is difficult to explain. As dehydration becomes more severe it is possible that compensatory mechanisms may fail giving rise to a change in the nature of the relationship. Physiological volume regulation of intra-cranial compartments is likely to be complex and a definitive explanation of this relationship is beyond the scope of this study.

Although we showed a clear correlation between dehydration and ventricular volume there was no correlation between dehydration and brain volume. The mean pre-dehydration ventricular volume of the six subjects was 20 429 mm^3 (SD = 6124) and the mean magnitude of the change in ventricular volume was 2634 mm^3 (SD = 2281). Therefore the mean percentage change was 11.6%. The mean pre-dehydration brain volume for each of the six subjects was 1 003 990 mm^3 and therefore the change in ventricular volume expressed as a percentage of brain volume is 0.26%. Such small percentage changes are unlikely to show statistically significant correlations and probably explain why there was no correlation between dehydration and total brain volume.

T_1-weighted MRI scanning gives the best possible anatomical resolution however it does not permit measurement of the volume of the subarachnoid space using the point counting technique. Since intra-cranial volume equals the sum of the volumes of the brain, the intra-cranial CSF (intra-ventricular volume plus subarachnoid CSF volume), and the intra-cranial blood, a value for the volume of the CSF in the subarachnoid space would have enabled us to draw definitive conclusions about changes in the other intra-cranial compartments. The use of T_2-weighted scans would avoid this problem in further studies.

In conclusion, we have shown for the first time that dehydration causes changes in the volume of intra-cranial compartments. This may put sportsmen and women at increased risk of brain damage from contusion injuries and dural border cell haematomas (commonly referred to as sub-dural haemorrhages) after head injuries. Some sportsmen and women e.g., boxers, rugby players, and footballers are especially vulnerable to serious head injuries whilst dehydrated. The present study is too small to draw definitive conclusions about the effects of dehydration on

each intra-cranial compartment and the physiological basis of these changes but the implications for the outcome of head injuries merits further investigation in a larger systematic study.

Acknowledgements

Many thanks to Paul Vaughn for all his help transferring and relabelling the scans. Thanks to the radiographers at the Academic Radiology Unit, especially Dave Capener. These data have been presented as an abstract at the British Association of Sport and Exercise Sciences, Student Conference, Coventry (2003).

References

[1] Cutler R. Formation and absorption of cerebrospinal fluid in man. Brain 1968; 91: 707
[2] Bull J. The volume of the cerebral ventricles. Neurology 1961; 11: 1
[3] Mokri B. The Monro-Kellie hypothesis. Applications in CSF volume depletion. Neurology 2001; 56: 1746 – 1748
[4] Gullans S, Verbalis J. Control of brain volume during hyperosmolar and hypo-osmolar conditions. Ann Rev Med 1993; 44: 289 – 301
[5] Lee R, Abraham R, Quinn C. Dynamic physiologic changes in lumbar CSF volume quantitatively measured by three-dimensional fast spin-echo MRI. Spine 2001; 26: 1172 – 1178
[6] Besenski N. Traumatic injuries: imaging of head injuries. Eur Radiol 2002; 12: 1237 – 1252
[7] Servadei F, Murray G, Teasdale G, Dearden M, Iannotti F, Lapierre F et al. Traumatic subarachnoid hemorrhage: demographic and clinical study of 750 patients from the European brain injury consortium survey of head injuries. Neurosurgery 2002; 50: 261 – 267
[8] Robb R. Analyze Reference Manual v 6.2; 1986