# nature research

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# **Reporting Summary**

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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n/a	Confirmed
	$\square$ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	The statistical test(s) used AND whether they are one- or two-sided  Only common tests should be described solely by name; describe more complex techniques in the Methods section.
	A description of all covariates tested
	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
	Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i> ), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

# Software and code

Policy information about availability of computer code

Data collection

We have used the MRI files of the subjects, and we prepared all of these data according to the ethical standards of the Shohada Tajrish Hospital.

Data analysis

We have used ADINA 8.3 (Adina R&D Inc., Watertown MA, USA) software for data analysis. However, we used the routine toolbar of this software and we didn't use any specific codes.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

### Data

Policy information about <u>availability of data</u>

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

For data validation, we compared the computer simulation data with experimental data of ICP-monitoring and also invivo CSF velocity data. We listed the results of these comparisons in the Table 1 and Fig.1f and g, and also Fig. 3a-c. The MRI files of subjects contain some identifying information of patients and normal subjects, and cannot be made publicly available. All relevant data are available from the corresponding author upon request. Raw data for Fig. 1a and Fig. 3a-c are included in Supplementary Data files 1 and 2, and raw data for Fig. 3d-g is also included in Tables 2 and 3.

Field-specific reporting			
<u>-</u>		s the best fit for your research. If you are not sure, read the appropriate sections before making your selection.	
Life sciences		Behavioural & social sciences	
		all sections, see <a href="mailto:nature.com/documents/nr-reporting-summary-flat.pdf">nature.com/documents/nr-reporting-summary-flat.pdf</a>	
Life scier	nces stu	udy design	
All studies must dis	close on these	points even when the disclosure is negative.	
Sample size	eight healthy su	ubjects and 11 hydrocephalus patients	
Data exclusions	(N/A): no data	were excluded	
Replication	All attempt at r	replication were successful	
Randomization	Allocation of su	ubjects was random	
Blinding	Prior to scannir for analysis.	ng, written informed consent was obtained from all the volunteers. All MRI data were anonymized prior to transfer to operators	
Reportin	g for sp	pecific materials, systems and methods	
We require information	on from authors	about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.	
Materials & exp			
n/a Involved in th	-	n/a Involved in the study	
Antibodies	,	ChIP-seq	
Eukaryotic	Eukaryotic cell lines Flow cytometry		
Palaeontol	ogy and archaeo	logy MRI-based neuroimaging	
Animals an	nd other organism	ns	
☐ X Human res	Human research participants		
Clinical data			
Dual use re	esearch of concer	'n	
Antibodies			
Antibodies used			
Validation	Validation We had data validation section, however, we did not use any antibody		
Eukaryotic cell lines			
Policy information about cell lines			
Cell line source(s	)	(N/A): We did not use any cell line source	
Authentication		(N/A): We did not use any cell line source	
Mycoplasma con	tamination	(N/A): We did not use any cell line source	
Commonly misidentified lines (See ICLAC register)  (N/A): We did not use any cell line source		(N/A): We did not use any cell line source	

# Palaeontology and Archaeology

Specimen provenance (N/A)

Consissor describing	(A) (A)		
Specimen deposition			
Dating methods	(N/A): No new dates are provide		
Tick this box to confir	m that the raw and calibrated dates are available in the paper or in Supplementary Information.		
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.		
Note that full information on t	ne approval of the study protocol must also be provided in the manuscript.		
Animals and othe	r organisms		
Policy information about <u>st</u>	udies involving animals; ARRIVE guidelines recommended for reporting animal research		
Laboratory animals	(N/A): This study did not involve laboratory animals		
Wild animals	(N/A): This study did not involve laboratory animals		
Field-collected samples	(N/A): This study did not involve laboratory animals		
Ethics oversight	(N/A): This study did not involve laboratory animals		
Note that full information on t	ne approval of the study protocol must also be provided in the manuscript.		
Human research (	participants		
Policy information about <u>st</u>	udies involving human research participants		
Population characteristic:	11 hydrocephalus patients and eight healthy subjects were recruited. The age range of the patients (six males and five females) and the healthy subjects (four males and four females) was 53-74 and 48-69 years, respectively. Moreover, the range of the body mass index of the patients and the healthy subjects was 23.8-29.4 and 25.0-30.2, respectively. Shohada Tajrish Neurosurgical team diagnose and treated these patients.		
Recruitment	11 patients and eight healthy subjects were recruited from a total of 42 hydrocephalus patients and 23 healthy subjects based on their age range and BMI.		
Ethics oversight	the data access and ethics committees of Shohada Tajrish Neurosurgical Centre of Excellence.		
Note that full information on t	ne approval of the study protocol must also be provided in the manuscript.		
Clinical data			
Policy information about <u>cl</u>	nical studies with the ICMJE <u>guidelines for publication of clinical research</u> and a completed <u>CONSORT checklist</u> must be included with all submissions.		
Clinical trial registration	(N/A): This study was not Clinical trial		
Study protocol	(N/A): This study was not Clinical trial		
	(N/A): This study was not Clinical trial		
Data collection	(N/A): This study was not Clinical trial		
Outcomes (N/A): This study was not Clinical trial			
Dual use research of concern			
Policy information about <u>dual use research of concern</u>			
Hazards			
Could the accidental, deli	berate or reckless misuse of agents or technologies generated in the work, or the application of information presented		
No   Yes			
Public health			
National security			
Crops and/or livest	ock		
Ecosystems  Any other significa	nt area		
<u>-</u>			

<u> </u>				
Experiments of concer				
1	y of the	ese experiments of concern:		
	No Yes			
		er a vaccine ineffective		
		peutically useful antibiotics or antiviral agents		
		pathogen or render a nonpathogen virulent		
Increase transmiss	•			
	Alter the host range of a pathogen			
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		of a biological agent or toxin		
Any other potentia	illy narm	ful combination of experiments and agents		
ChIP-seq				
Data deposition				
	v and fii	nal processed data have been deposited in a public database such as <u>GEO</u> .		
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Confirm that you have	e aepos	ited or provided access to graph files (e.g. BED files) for the called peaks.		
Data access links May remain private before publi	cation.	We create our data base with regards to all policy of our ethical approval and data access committee. According to this policy for accessing the data should contact with corresponding author		
Files in database submission		We create our data base with regards to all policy of our ethical approval and data access committee. According to this policy for accessing the data should contact with corresponding author		
Genome browser session (e.g. <u>UCSC</u> )		We create our data base with regards to all policy of our ethical approval and data access committee. According to this policy for accessing the data should contact with corresponding author		
Methodology				
Replicates	First, the CSF velocity diagram in CA calculated from the FSI simulation of each healthy subject and each patient was compared with the CSF velocity diagram in CA which was measured experimentally using the CINE phase-contrast magnetic resonance imaging (CINE PC-MRI) of them. Second, the values of CSF pressure in SAS were experimentally measured in 10 of the 11 patients by ICP monitoring were compared with CSF pressure calculated from the FSI simulation. All experimental test were repeated five times.			
Sequencing depth	All experimental test were repeated five times. It should be noted the time and length of tests were not important and effective in the tests.			
Antibodies	(N/A): No antibodies were used in the tests.			
Peak calling parameters	(N/A): No command line program and were used in the tests.			
Data quality	For insurance about correctness of our data we have compared our computer simulation data with the experimental data (CINE PC-MRI and ICP monitoring).			
Software	DICOM files obtained from MRI of each healthy subject and patient were transferred to Mimics software v13.1 to prepare the points cloud that the points in the cloud were voxel centres. The point clouds of the head substructures (SAS, brain tissue, and ventricular system) were produced for each healthy subject and patient and transferred to CATIA v5.R21 for 3D geometrical modeling. After creating 3D geometrical models of the head of the healthy subjects and patients separately (Fig. 4d), the models were transferred to ADINA 8.3 (Adina R&D Inc., Watertown MA, USA) for meshing (Fig. 4e) and analysis. It should be noted that we only used the routine toolbars of these softwares and we did not write any programming.			
Flow Cytometry				

Ч	lots	

Confirm that:
The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
All plots are contour plots with outliers or pseudocolor plots.
A numerical value for number of cells or percentage (with statistics) is provided.

## Methodology

Software

Sample preparation
Accordingly, 11 patients and eight healthy subjects were recruited.

Instrument
MRI

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DICOM files obtained from MRI of each healthy subject and patient were transferred to Mimics software v13.1 to prepare the points cloud that the points in the cloud were voxel centres. The point clouds of the head substructures (SAS, brain tissue, and ventricular system) were produced for each healthy subject and patient and transferred to CATIA v5.R21 for 3D geometrical modeling. After creating 3D geometrical models of the head of the healthy subjects and patients separately (Fig. 4d), the models were transferred to ADINA 8.3 (Adina R&D Inc., Watertown MA, USA) for meshing (Fig. 4e) and analysis. It should be noted that we only used the routine toolbars of these softwares and we did not write any programming.

Cell population abundance (N/A): We did not use Cell in our study

Gating strategy (N/A): We did not use Cell in our study

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

# Magnetic resonance imaging

# Experimental design

Design type We used event-relevant

Design specifications

Each tests were repeated for 5 times. Scanning was performed using a 3 Tesla MRI system (Magnetom Trio, Siemens, Erlangen, Germany), with the acquisition time of 45 minutes.

Behavioral performance measures Each tests were repeated for 5 times. We calculated the mean, SD, confidence interval and coefficient of variation.

# Acquisition

Imaging type(s)

We used structural imaging

Field strength Scanning was performed using a 3 Tesla MRI system (Magnetom Trio, Siemens, Erlangen, Germany)

Sequence & imaging parameters

A velocity encoding value (VENC) of 100 cm/s was chosen to measure the CSF flow. Further parameters used in the measurement included: repetition time = 18 msec; flip angle = 23°; echo time = 8.3 msec; field of view = 23 cm; slice thickness = 3 mm; and matrix size = 256×198. The pixel velocity in CSF areas was corrected by subtracting the average velocity of solid brain tissue in a nearly 29×29 mm2 area surrounding the pixel.

Area of acquisition
The pixel velocity in CSF areas was corrected by subtracting the average velocity of solid brain tissue in a nearly 29×29 mm2 area surrounding the pixel.

Diffusion MRI Used Not used

## Preprocessing

Preprocessing software

DICOM files obtained from MRI of each healthy subject and patient were transferred to Mimics software v13.1 to prepare the points cloud that the points in the cloud were voxel centres. The point clouds of the head substructures (SAS, brain tissue, and ventricular system) were produced for each healthy subject and patient and transferred to CATIA v5.R21 for 3D geometrical modeling. After creating 3D geometrical models of the head of the healthy subjects and patients separately (Fig. 4d), the models were transferred to ADINA 8.3 (Adina R&D Inc., Watertown MA, USA) for meshing (Fig. 4e) and analysis. It should be noted that we only used the routine toolbars of these softwares and we did not write any programming.

Normalization

The inlet of BC "B" and inlet and outlets of BC "C" were calculated with the superposition of a constant value of flow rate and the normalized pulsatile profile of the blood flow rate in the basilar artery, which was measured with the CINE PC-MRI for all the healthy subjects and hydrocephalus patients. The process of normalization were calculated using MATLAB software.

We only used the MATLAB toolbars for normalizing the flow rate function of the blood for inlet inlet of BC "B" and inlet and outlets of BC "C".

Noise and artifact removal (N/A): We did not use the noise removing process.

Volume censoring (N/A): We did not use volume censoring

#### Statistical modeling & inference

Model type and settings

Normalization template

Pearson correlation coefficient (PCC) was used in the present study to assess the correlation between the maximum CSF pressure in SAS and the ventricular system volume (two effective and accurate indices) under the three inlet/outlet BCs for 11 patients.

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Effect(s) tested	(N/A): We have not need to assess the effects test	
Specify type of analysis: 🔀 Whole brain 🗌 ROI-based 📗 Both		
Statistic type for inference (See Eklund et al. 2016)	(N/A): We have not need to assess voxel/cluster-wise.	
Correction (N/A): We have not need to assess the correction.		
Models & analysis  n/a   Involved in the study  Functional and/or effective  Graph analysis  Multivariate modeling or p		
Graph analysis	The results of the Shapiro-Wilk test showed that the datasets had a normal distribution. Parametric ANOVA	

The results of the Shapiro-Wilk test showed that the datasets had a normal distribution. Parametric ANOVA Multiple Comparison was used [99] to compare the CSF pressure, the aqueductal CSF stroke volume, the Reynolds number, the CSF velocity, and the volume between healthy subjects and patients under the three BCs "A", "B", and "C". The homogeneity of the variance test showed that all the variances were equal. Hence, Tukey's post-hoc test was used for pair-wise comparison after ANOVA when comparing the data under the three BCs. Moreover, the normally distributed data led to using Student's t-test after ANOVA to compare both groups of CSF velocities obtained from computer simulation and CINE PC-MRI, and two groups of CSF pressures obtained from computer simulation and ICP-monitoring for assessing data validation. Student's t-test with equal variance was also used to compare the CSF pressure results of CFD and FSI simulations. The test statistics for ANOVA and Student's t-test were T and F, respectively.

The PCC, a number between -1 and +1, is an index for evaluating the correlation between two phenomena [100]. Hence, after ensuring the normal distribution of the data, PCC was used to assess the correlation between the maximum CSF pressure and the ventricular system volume under the three BCs. The data were described as mean±SE, and the P-value of 0.05 was considered statistically significant.