Supplementary Material

Cerebrospinal fluid volumetric net flow rate and direction in idiopathic normal pressure hydrocephalus

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(a)
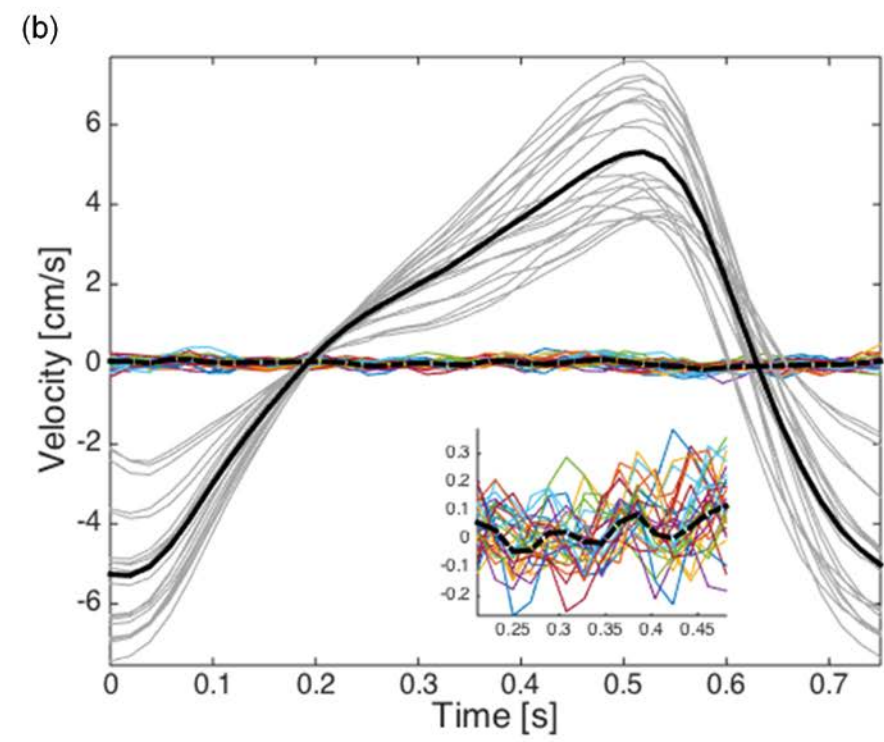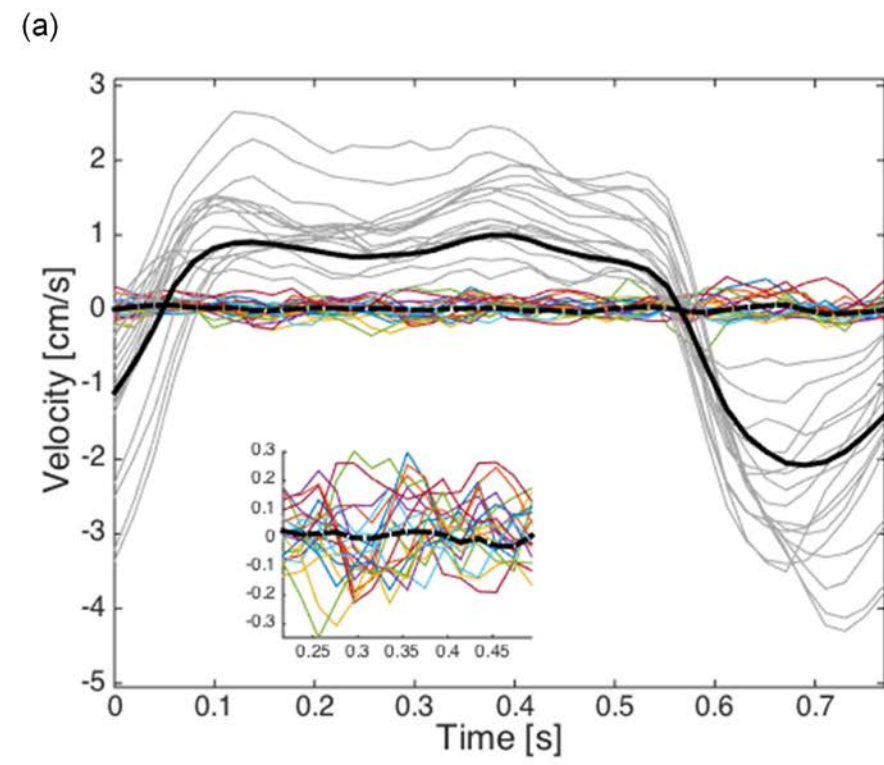
Suppl Fig. 1. Determining mean velocities of CSF flow in CCJ and cerebral aqueduct regions (ID13).
For (a) the CCJ and (b) the cerebral aqueduct, the black solid line indicates mean velocity and grey lines the pixel velocities. The black dashed line indicates the mean velocity (bias) of reference ROI pixels and the colored lines pixel velocities in reference ROI (noise). Note that for CCJ only 17 pixels out of 484 pixels were included for illustrative purpose only.

(b)
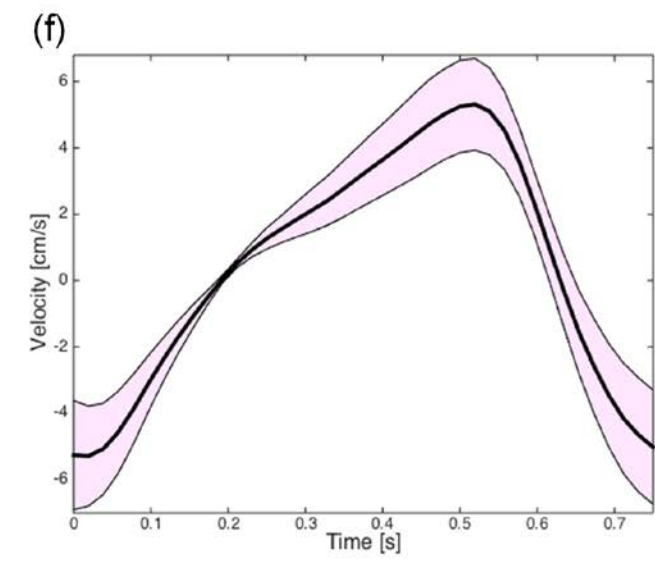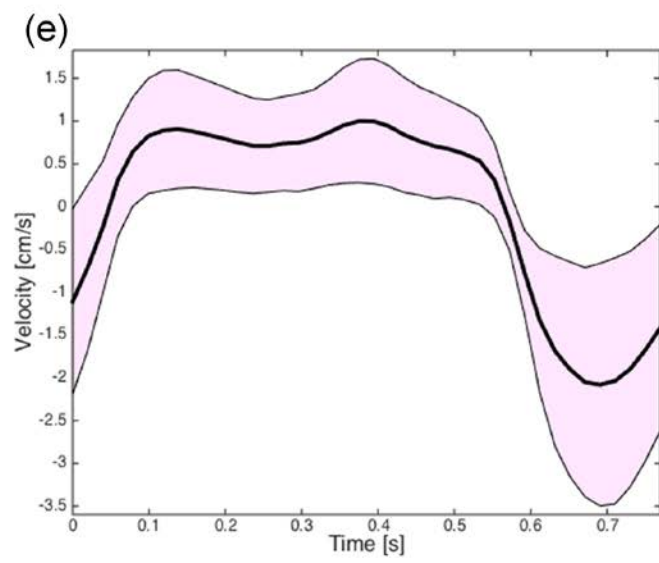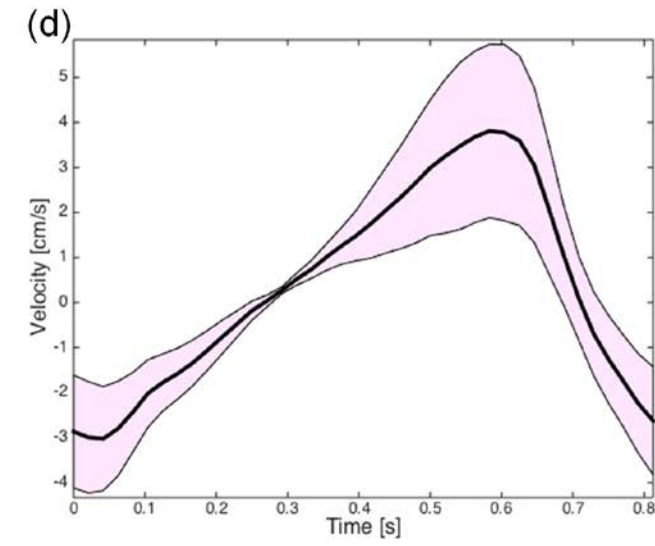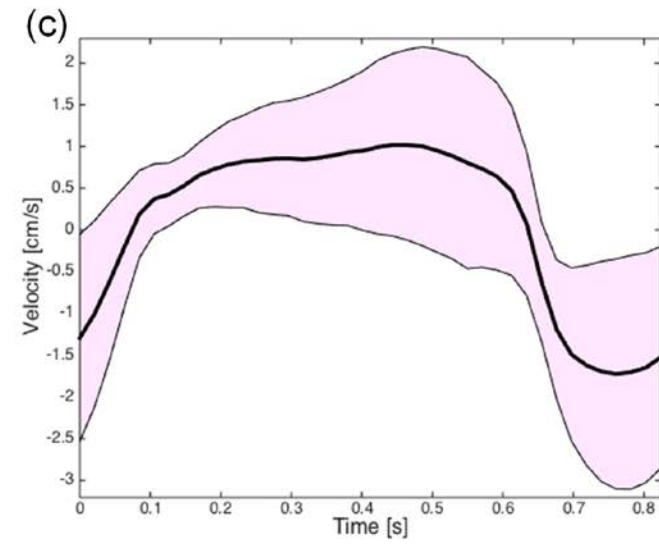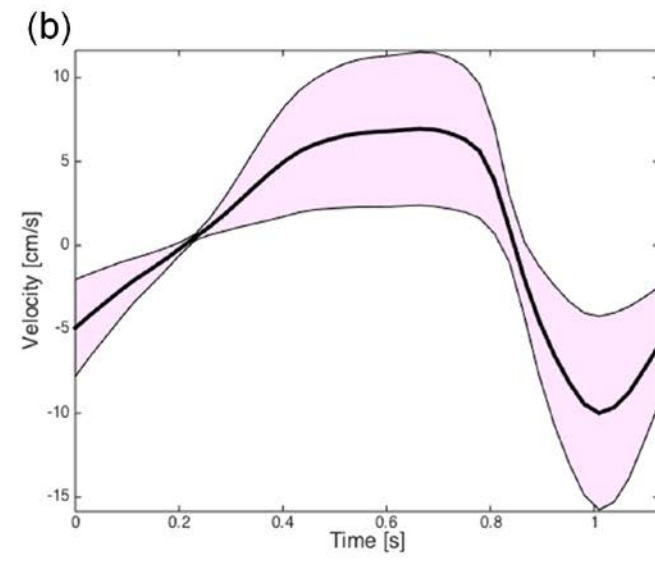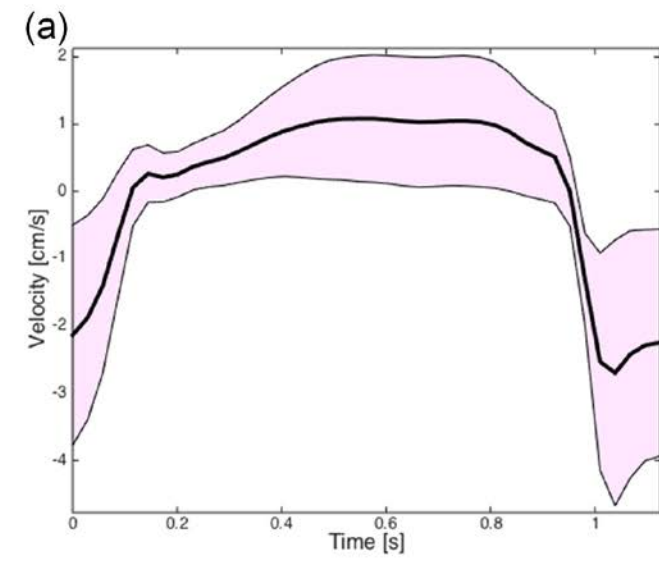
Suppl Fig. 2. Mean and standard deviation of CSF flow velocities in CCJ and aqueduct of iNPH patients (IDs 3, 6, and 13). The mean velocities (black line) with standard deviations (pink background) are shown for CCJ (a, c, e) and cerebral aqueduct (b, d, f) of three iNPH individuals (IDs 3 a-b, 6 c-d, and 13 e-f) to illustrate variability between cases.

Suppl Table 1. Demographic information of individual iNPH patients and healthy subjects

PatID	Category	Age (yrs)	Gender		MRI biomarkers			iNPH category		
			M	F	Evan's index	Callosal angle	DESH	Responder	Non-responders	Conservative
1	iNPH	56	1		0.33	90	0	1		
2	iNPH	70		1	0.31	116	0			1
3	iNPH	63	1		0.33	77	0	1		
4	iNPH	66		1	0.42	131	0	1		
5	iNPH	55	1		0.42	120	0	1		
6	iNPH	82	1		0.39	55	0	1		
7	iNPH	74	1		0.37	55	1	1		
8	iNPH	75		1	0.39	68	1	1		
9	iNPH	71	1		0.39	65	1	1		
10	iNPH	79		1	0.39	62	1	1		
11	iNPH	78		1	0.39	89	1			1
12	iNPH	70		1	0.38	121	0	1		
13	iNPH	75	1		0.38	98	1	1		
14	iNPH	60	1		0.38	66	1			1
15	iNPH	45	1		0.35	123	0			1
16	iNPH	71	1		0.47	68	0	1		
17	iNPH	65		1	0.36	100	0	1		
18	iNPH	84	1		0.29	122	0		1	
19	iNPH	59		1	0.43	130	0			1
20	iNPH	72		1	0.36	84	1		1	
21	iNPH	79	1		0.38	85	1			1
22	iNPH	77		1	0.41	75	1	1		
23	iNPH	76		1	0.32	114	1	1		
24	iNPH	73	1		0.34	52	1	1		
25	iNPH	80	1		0.48	78	1	1		
26	iNPH	60	1		0.36	62	0			1
1	Healthy	40	1		0.28	104	0			
2	Healthy	36		1	0.25	90	0			
3	Healthy	23	1		0.25	110	0			
4	Healthy	24	1		0.27	102	0			

iNPH: idiopathic normal pressure hydrocephalus; DESH: disproportionately enlarged subarachnoid space hydrocephalus.

Suppl Table 2. CSF flow volume data within CCJ of individual iNPH patients and healthy subjects

PatID	Category	ROI (cm2)	ROI (pix)	SNR (pix-by-pix)	dP (mmHg/cm)	Volumetric net flow rate (ml/cycle)	Tot volumetric flow rate (ml/ cycle)	Estimated volumetric net flow rate(L/24 hrs)	Max velocity (cranial, cm/s)	Min velocity (caudal, cm/s)	[a]Direction of net flow
1	iNPH	2.281	584	17.687	0.046	0.176	1.322	17.89	0.740	-1.421	C
2	iNPH										
3	iNPH	1.969	504	24.271	0.056	0.180	2.396	13.82	1.056	-2.797	C
4	iNPH	1.398	358	19.834	0.049	0.039	0.988	4.34	0.894	-1.886	C
5	iNPH	1.481	379	20.557	0.070	0.044	2.340	3.55	1.384	-3.253	C
6	iNPH	1.352	346	20.715	0.041	0.095	1.111	9.98	0.980	-1.772	C
7	iNPH	1.309	335	61.026	0.054	0.139	1.094	14.37	1.175	-1.750	C
8	iNPH										
9	iNPH	2.500	640	12.935	0.027	0.249	1.804	20.58	0.775	-1.279	C
10	iNPH										
11	iNPH	1.848	473	60.143	0.032	0.292	1.725	26.75	1.095	-1.794	C
12	iNPH	1.590	407	12.912	0.015	0.185	0.532	18.05	0.408	-0.588	C
13	iNPH	1.891	484	19.353	0.044	0.057	1.498	6.42	0.986	-2.117	C
14	iNPH	2.133	546	11.039	0.036	0.122	1.054	16.53	0.820	-1.407	C
15	iNPH	1.195	306	25.916	0.083	-0.040	2.159	-3.33	2.275	-3.938	S
16	iNPH	1.270	325	20.176	0.032	-0.054	1.444	0.84	1.231	-2.006	C
17	iNPH	1.648	422	26.363	0.045	0.008	2.064	0.67	1.049	-2.739	C
18	iNPH	1.879	481	15.999	0.035	0.030	1.210	3.16	0.693	-1.342	C
19	iNPH	1.195	306	30.028	0.080	0.010	1.564	1.05	1.449	-3.811	C
20	iNPH	1.836	470	13.085	0.026	-0.068	1.448	-5.61	0.453	-1.485	S
21	iNPH										
22	iNPH	1.633	418	17.465	0.042	0.029	1.278	2.94	0.926	-1.676	C
23	iNPH	1.621	415	7.833	0.016	-0.002	0.341	-0.17	0.277	-0.643	S
24	iNPH	3.496	895	20.786	0.040	-0.009	1.694	-1.12	0.838	-1.547	S
25	iNPH	1.953	500	95.029	0.052	-0.048	0.989	-5.36	0.773	-1.863	S
26	iNPH	2.387	611	103.697	0.039	0.066	1.852	5.66	1.006	-2.007	C
Average ± std		1.81 ± 0.53	463.9 ± 136.4	29.86 ± 26.18	0.044 ± 0.018	0.068 ± 0.101	1.450 ± 0.535	6.864 ± 9.042	0.967 ± 0.412	-1.960 ± 0.873	
1	Healthy	0.720	233.2	34.953	0.093	0.033	1.284	3.27	2.371	-4.038	C
2	Healthy	1.350	437.4	49.013	0.045	0.014	1.052	1.42	1.036	-1.994	C
3	Healthy	1.244	403.0	48.386	0.065	0.112	1.818	9.02	1.800	-3.539	C
4	Healthy	1.530	495.6	42.174	0.032	0.164	1.300	11.89	0.931	-1.821	C
Average ± std		1.21 ± 0.35	392.3 ± 112.7	43.631 ± 6.558	0.059 ± 0.027	0.081 ± 0.070	1.363 ± 0.323	6.399 ± 4.881	1.534 ± 0.679	-2.848 ± 1.107	

[a]Direction of net flow: C=Cranially directed; S=Spinally directed. ROI (cm2): Size of region of interest in cm^2. ROI (pix): Size of region of interest in number of pixels. SNR (pix-by-pix): Signal to noise ratio calculated pixel by pixel. dP (mmHg/cm): Pressure gradient calculated from PC-MRI measurements. Net vol/cycle (ml): Bias corrected net volume of CSF during one cardiac cycle. Tot vol/cycle (ml): Bias corrected total volume of CSF during one cardiac cycle. Net vol/day (l): Sum of net vol/cycle during 24 hours. Max velocity (cranial, cm/s): Peak velocity in cranial direction extracted from mean velocities. Min velocity (caudal, cm/s): Peak velocity in caudal direction extracted from mean velocities.

Suppl Table 3. CSF flow volume data within cerebral aqueduct of individual iNPH patients and healthy subjects

PatID	Category	ROI (cm2)	ROI (pix)	SNR (pix-by-pix)	dP (mmHg/cm)	Volumetric net flow rate (ml/cycle)	Tot volumetric flow rate (ml/ cycle)	Estimated volumetric net flow rate (L/24 hrs)	Max velocity (cranial, cm/s)	Min velocity (caudal, cm/s)	[a]Direction of net flow
1	iNPH	0.150	50	23.105	0.057	0.016	0.194	1.66	2.073	-3.315	R
2	iNPH	0.108	36	29.161	0.073	-0.002	0.272	-0.22	4.511	-5.608	A
3	iNPH	0.117	39	33.569	0.138	0.072	0.659	5.53	6.941	-9.899	R
4	iNPH										
5	iNPH										
6	iNPH	0.108	36	24.264	0.061	0.034	0.169	3.59	3.778	-3.003	R
7	iNPH	0.093	31	23.344	0.097	0.021	0.211	2.20	5.213	-4.574	R
8	iNPH	0.096	32	30.715	0.091	0.024	0.280	2.30	4.719	-6.097	R
9	iNPH	0.066	22	30.212	0.087	0.020	0.286	1.66	6.446	-7.690	R
10	iNPH	0.048	16	30.496	0.132	0.009	0.142	1.17	6.289	-7.439	R
11	iNPH	0.030	10	25.630	0.041	0.006	0.057	0.53	3.566	-3.440	R
12	iNPH										
13	iNPH	0.063	21	28.615	0.089	0.023	0.144	2.63	5.312	-5.326	R
14	iNPH	0.233	78	22.561	0.050	-0.002	0.270	-0.25	3.431	-3.027	A
15	iNPH										
16	iNPH	0.269	90	30.532	0.089	0.044	1.072	3.98	5.813	-7.450	R
17	iNPH	0.075	25	33.143	0.111	0.049	0.375	3.92	6.435	-9.505	R
18	iNPH	0.075	25	32.163	0.089	0.004	0.193	0.39	4.472	-5.914	R
19	iNPH										
20	iNPH	0.096	32	36.264	0.201	0.019	0.753	1.58	9.626	-15.983	R
21	iNPH	0.108	36	28.266	0.111	-0.037	0.338	-4.10	5.954	-7.322	A
22	iNPH	0.153	51	32.400	0.116	-0.009	0.605	-0.89	6.720	-9.147	A
23	iNPH	0.040	17	12.907	0.041	-0.003	0.043	-0.27	1.465	-2.426	A
24	iNPH	0.076	32	29.583	0.188	0.001	0.331	0.08	7.838	-11.553	R
25	iNPH	0.069	29	16.205	0.070	-0.001	0.117	-0.11	3.181	-4.165	A
26	iNPH	0.028	12	29.269	0.103	-0.028	0.140	-2.45	5.468	-11.161	A
Average ± std		**0.100 ± 0.061**	**34.286 ± 19.807**	**27.734 ± 5.716**	**0.097 ± 0.042**	**0.012 ± 0.025**	**0.317 ± 0.256**	**1.091 ± 2.239**	**5.202 ± 1.924**	**-6.859 ± 3.451**	
1	Healthy	0.023	9.8	21.887	0.058	-0.002	0.047	-0.24	3.777	-4.198	A
2	Healthy	0.017	7.2	16.443	0.032	-0.003	0.017	-0.34	1.712	-2.125	A
3	Healthy	0.038	16	24.241	0.096	-0.002	0.113	-0.22	6.122	-4.867	A
4	Healthy	0.014	6	14.750	0.032	-0.003	0.018	-0.26	1.423	-2.371	A
Average ± std		**0.0238 ± 0.011**	**9.75 ± 4.46**	**19.330 ± 4.471**	**0.055 ± 0.031**	**-0.003 ± 0.001**	**0.049 ± 0.045**	**-0.263 ± 0.051**	**3.259 ± 2.178**	**-3.390 ± 1.351**	

[a]Direction of net flow: A=Antegrade; R=Retrograde.

Suppl Table 4. CSF flow volume data within CCJ of healthy subjects for repeated MRI acquisitions

PatID	MRI scan no	ROI (cm2)	ROI (pix)	SNR (pix-by-pix)	dP (mmHg/cm)	Volumetric net flow rate (ml/cycle)	Tot volumetric flow rate (ml/ cycle)	Estimated volumetric net flow rate (L/24 hrs)	Max velocity (cranial, cm/s)	Min velocity (caudal, cm/s)	[a]Direction of net flow
1	1	0.787	255	30.730	0.100	0.001	1.340	0.085	2.195	-4.226	C
	2	0.688	223	31.049	0.094	0.029	1.238	2.899	2.530	-4.128	C
	3	0.731	237	35.978	0.093	0.106	1.162	10.577	2.198	-3.791	C
	4	0.698	226	32.070	0.092	-0.046	1.346	-4.377	2.376	-4.097	S
	5	0.694	225	44.937	0.085	0.077	1.334	7.185	2.556	-3.949	C
Average ± std		**0.720 ± 0.041**	**233.2 ± 13.3**	**34.953 ± 5.960**	**0.093 ± 0.005**	**0.033 ± 0.060**	**1.284 ± 0.081**	**3.274 ± 5.863**	**2.371 ± 0.174**	**-4.038 ± 0.170**	
2	1	1.219	395	49.456	0.034	0.047	0.984	4.357	1.078	-1.851	C
	2	1.441	467	48.130	0.043	-0.014	1.194	-1.335	1.031	-2.100	S
	3	1.429	463	49.249	0.048	0.011	1.190	1.045	0.965	-2.069	C
	4	1.219	395	50.008	0.050	0.039	0.826	4.376	1.078	-1.851	C
	5	1.441	467	48.222	0.049	-0.012	1.064	-1.327	1.031	-2.100	S
Average ± std		**1.350 ± 0.120**	**437.4 ± 38.7**	**49.013 ± 0.814**	**0.045 ± 0.007**	**0.014 ± 0.028**	**1.052 ± 0.154**	**1.423 ± 2.856**	**1.036 ± 0.046**	**-1.994 ± 0.131**	
3	1	1.420	460	42.834	0.052	0.011	1.880	1.038	1.638	-3.159	C
	2	1.262	409	45.313	0.042	0.287	1.956	22.165	1.537	-2.910	C
	3	1.324	429	49.141	0.079	0.021	1.475	2.144	1.880	-3.329	C
	4	1.099	356	51.806	0.074	0.113	1.961	8.703	2.026	-4.137	C
	5	1.114	361	52.835	0.079	0.130	1.817	11.026	1.918	-4.158	C
Average ± std		**1.244 ± 0.137**	**403.0 ± 44.5**	**48.386 ± 4.252**	**0.065 ± 0.017**	**0.112 ± 0.111**	**1.818 ± 0.201**	**9.015 ± 8.484**	**1.800 ± 0.204**	**-3.539 ± 0.576**	
4	1	1.698	550	43.470	0.031	0.183	1.376	13.577	0.876	-1.812	C
	2	1.401	454	42.794	0.032	0.195	1.217	14.790	1.024	-1.833	C
	3	1.389	450	45.158	0.038	0.069	1.218	5.109	0.973	-2.005	C
	4	1.534	497	36.143	0.027	0.186	1.309	12.448	0.798	-1.623	C
	5	1.627	527	43.303	0.030	0.189	1.380	13.502	0.984	-1.835	C
Average ± std		**1.530 ± 0.136**	**495.6 ± 44.0**	**42.174 ± 3.486**	**0.032 ± 0.004**	**0.164 ± 0.054**	**1.300 ± 0.081**	**11.885 ± 3.878**	**0.931 ± 0.092**	**-1.821 ± 0.136**	

[a]Direction of net flow: A=Antegrade; R=Retrograde.

Suppl Table 5. CSF flow volume data within cerebral aqueduct of healthy subjects for repeated MRI acquisitions

PatID	MRI scan no	ROI (cm2)	ROI (pix)	SNR (pix-by-pix)	dP (mmHg/cm)	Volumetric net flow rate (ml/cycle)	Tot volumetric flow rate (ml/ cycle)	Estimated volumetric net flow rate (L/24 hrs)	Max velocity (cranial, cm/s)	Min velocity (caudal, cm/s)	[a]Direction of net flow
1	1	0.021	9	23.008	0.065	-0.002	0.046	-0.187	4.092	-4.598	A
	2	0.021	9	21.847	0.057	0.000	0.043	-0.017	3.891	-4.241	A
	3	0.021	9	22.080	0.063	-0.006	0.042	-0.636	3.698	-4.564	A
	4	0.024	10	22.031	0.056	-0.002	0.049	-0.176	3.776	-4.021	A
	5	0.028	12	20.467	0.050	-0.002	0.054	-0.195	3.427	-3.567	A
Average ± std		0.023 ± 0.003	9.8 ± 1.3	21.887 ± 0.912	0.058 ± 0.006	-0.002 ± 0.002	0.047 ± 0.005	-0.242 ± 0.232	3.777 ± 0.245	-4.198 ± 0.426	
2	1	0.017	7	15.593	0.028	-0.003	0.016	-0.299	1.541	-2.004	A
	2	0.017	7	16.854	0.028	-0.005	0.017	-0.496	1.536	-2.159	A
	3	0.017	7	16.398	0.032	-0.005	0.017	-0.483	1.567	-2.047	A
	4	0.019	8	15.940	0.033	-0.003	0.016	-0.289	1.810	-2.145	A
	5	0.017	7	17.431	0.036	-0.001	0.016	-0.115	2.108	-2.268	A
Average ± std		0.017 ± 0.001	7.2 ± 0.4	16.443 ± 0.729	0.032 ± 0.003	-0.003 ± 0.002	0.017 ± 0.001	-0.336 ± 0.158	1.712 ± 0.249	-2.125 ± 0.104	
3	1	0.040	17	23.271	0.092	-0.002	0.097	-0.171	5.771	-4.375	A
	2	0.038	16	24.999	0.098	-0.003	0.108	-0.324	6.275	-5.121	A
	3	0.033	14	23.809	0.106	-0.009	0.083	-0.983	6.377	-4.810	A
	4	0.040	17	22.733	0.087	0.002	0.112	0.223	5.648	-3.838	R
	5	0.038	16	26.390	0.098	0.002	0.166	0.167	6.542	-6.192	R
Average ± std		0.038 ± 0.003	16.0 ± 1.2	24.241 ± 1.466	0.096 ± 0.007	-0.002 ± 0.005	0.113 ± 0.032	-0.218 ± 0.485	6.122 ± 0.391	-4.867 ± 0.884	
4	1	0.014	6	14.814	0.032	-0.004	0.019	-0.310	1.340	-2.623	A
	2	0.014	6	14.680	0.028	-0.003	0.017	-0.199	1.380	-2.049	A
	3	0.014	6	15.052	0.037	-0.004	0.017	-0.323	1.621	-2.364	A
	4	0.014	6	14.429	0.030	-0.002	0.017	-0.168	1.348	-2.325	A
	5	0.014	6	14.772	0.033	-0.004	0.020	-0.277	1.424	-2.492	A
Average ± std		0.014 ± 0.000	6.0 ± 0.0	14.750 ± 0.226	0.032 ± 0.003	-0.003 ± 0.001	0.018 ± 0.001	-0.255 ± 0.069	1.423 ± 0.116	-2.371 ± 0.214	

[a]Direction of net flow: A=Antegrade; R=Retrograde.

Suppl Table 6. ICP scores for individual iNPH patients.

PatID	Category	Mean ICP		MWA	
		Average (mmHg)	Percentage >15 mmHg for 30 sec	Average (mmHg)	Percentage >5 mmHg for 6 sec
1	iNPH	10.2	2	4.5	26
2	iNPH	7.7	0	5.2	58
3	iNPH	4.4	0	3.9	20
4	iNPH	4.6	0	4.0	14
5	iNPH	6.0	1	4.0	10
6	iNPH	3.4	0	4.7	27
7	iNPH	11.9	2	7.4	100
8	iNPH	8.2	0	6.3	70
9	iNPH	3.5	0	5.7	70
10	iNPH	6.6	0	7.9	96
11	iNPH	3.8	0	3.1	2
12	iNPH	6.7	0	5.7	71
13	iNPH	5.6	0	4.3	16
14	iNPH	3.0	0	3.4	4
15	iNPH	5.9	1	2.3	1
16	iNPH	9.7	2	3.9	22
17	iNPH	10.6	0	4.2	11
18	iNPH	6.5	0	3.5	2
19	iNPH	8.5	4	7.2	88
20	iNPH	-1.8	0	4.3	16
21	iNPH	8.8	0	3.5	1
22	iNPH	7.3	0	4.3	23
23	iNPH	5.1	0	5.9	76
24	iNPH	6.1	0	7.2	92
25	iNPH	10.3	15	4.9	42
26	iNPH	9.8	9	3.6	5
Average ± std		6.6 ± 3.0	1.4 ± 3.4	4.8 ± 1.5	37.1 ± 34.3