Cine phase-contrast MRI evaluation of normal aqueductal cerebrospinal fluid flow according to sex and age

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PURPOSE
The aim of this study was cerebrospinal flow quantification in the cerebral aqueduct using cine phase-contrast magnetic resonance imaging (MRI) technique in both sexes and five different age groups to provide normative data.

MATERIALS AND METHODS
Sixty subjects with no cerebral pathology were included in this study. Subjects were divided into five age groups: ≤14 years, 15–24 years, 25–34 years, 35–44 years, and ≥45 years. Phase, rephase, and magnitude images were acquired by 1.5 T MR unit at the level of cerebral aqueduct with spoiled gradient echo through-plane, which is a cine phase-contrast sequence. At this level, peak flow velocity (cm/s), average flow rate (cm/s), average flow (L/min), volumes in cranial and caudal directions (mL), and net volumes (mL) were studied.

RESULTS
There was a statistically significant difference in peak flow between the age group of ≤14 years and the older age groups. There were no statistically significant differences in average velocity, cranial and caudal volume, net volume, and average flow parameters among different age groups. Statistically significant differences were not detected in flow parameters between sexes.

CONCLUSION
When using cine-phase contrast MRI in the cerebral aqueduct, only the peak velocity showed a statistically significant difference between age groups; it was higher in subjects aged ≤14 years than those in older age groups. When performing age-dependent clinical studies including adolescents, this should be taken into consideration.

Key words: • magnetic resonance imaging, cine • cerebrospinal fluid • cerebral aqueduct

Magnetic resonance imaging (MRI) depicts cerebral tissue without need for contrast media in cerebral pathologies and gives detailed information on cerebrospinal fluid (CSF) and CSF flow pathways. In addition, physiopathologic evaluations including studies on CSF flow dynamics can be carried out by using cine-phase contrast techniques without need for invasive procedures such as contrast media injection or catheterization (1, 2).

Evaluation of CSF flow physiology and pathologies with cine-phase contrast MRI evaluation has gained momentum in the last 15 years. Studies using this technique, which is very sensitive even to slow flow, have focused on the ventricular system, subarachnoid spaces, spinal canal, and the cerebral aqueduct (3–5).

Following expression of flow through aqueduct quantitatively, an understanding of normal flow patterns was initially achieved, and flow changes in various pathologies were scrutinized. Communicating and obstructive hydrocephalus, Chiari malformation, and arachnoid cysts were the initial pathologies studied (6–9). Postsurgical clinical applications, such as evaluation of third ventriculostomy patency and aqueductal CSF flow evaluation following endoscopic aqueductoplasty came into use afterwards (10, 11). The characterization of normal CSF flow dynamics can provide pathophysiological information on diseases affecting CSF circulation by contributing to normal reference values.

In this study, aqueductal CSF flow parameters in different age groups were investigated using cine-phase contrast MRI technique, with the aim of measuring differences in flow parameters among age groups and sexes.

Materials and methods

In this six-month prospective study, 60 subjects who underwent imaging for other indications but were found to have no abnormalities were included. Written consent was obtained from all subjects or legal representatives of subjects before the procedures. Of the cases, 25 (41.6%) were female and 35 (58.3%) were males, with ages ranging from 6 years to 70 years (mean, 31.2). The individuals were divided into five age groups: ≤14 years, 15–24 years, 25–34 years, 35–44 years, and ≥45 years. The mean ages in groups were as follows respectively: 9.1 years, 20.1 years, 30.1 years, 40.3 years, and 57.7 years.

MRI examinations were performed with 1.5 T MR unit (Siemens Symphony, Erlangen, Germany). Imaging was carried out using standard head coils, in neutral supine position and without any case preparation. Subjects were asked to avoid deep breathing during the examination. Routine cranial axial and sagittal fast spin echo (FSE) T2-weighted images were acquired (TR/TE/NEX/FA, 5540/97/2/150˚; slice thickness, 5 mm; FOV, 250; matrix, 189 × 256).

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In all cases, cardiac gating was performed with MR compatible electrodes (Kendall, Arbo, Tyco International, Neustadt, Germany). A localizer was placed on cerebral aqueduct, perpendicular to ampullar region of the aqueduct on sagittal T2-weighted images; care was taken to be sure that the localizer line passed through the aqueductal plane on axial images. Using the above-mentioned T2-weighted image, axial images of spoiled gradient echo (SGE) through-plane sequence, which is the cine-phase contrast MRI sequence in the software, were acquired. The measurement parameters of this sequence were as follows: TR/TE/NEX/FA, 43/12/1/10°; slice thickness, 3 mm; gap, 1 mm; FOV, 160 mm; matrix,

192 × 256; duration, approx. 4 min. Velocity encoding (Venc) was selected as 20 cm/s in all cases. Directional programming was selected as positive for caudocranial direction and negative for craniocaudal direction in the software. Total examination duration was approximately fifteen minutes, including electrode placement, T2-weighted sequence, and SGE through-plane sequence acquisitions.

The acquired SGE through-plane images were transferred to Argus postprocessing program. In all cases, CSF flow was initially evaluated qualitatively following acquisitions of phase, rephase, and magnitude images. While the flow in the cerebral aqueduct had

high signal intensity in rephase and magnitude images, cranial flow had high signal intensity and caudal flow had low signal intensity in phase images. Images were magnified so the aqueduct could be seen optimally. As the flow and the contrast between the aqueduct and the adjacent cerebral structures were more prominent in rephase and magnitude images, a circular region of interest (ROI) was placed carefully on each image manually in one of those series. CSF flow changes throughout one cardiac cycle were extracted automatically from the program by velocity-time, peak velocity-time, flow-time, and net flow-time graphics (Fig.). In these graphics, the area
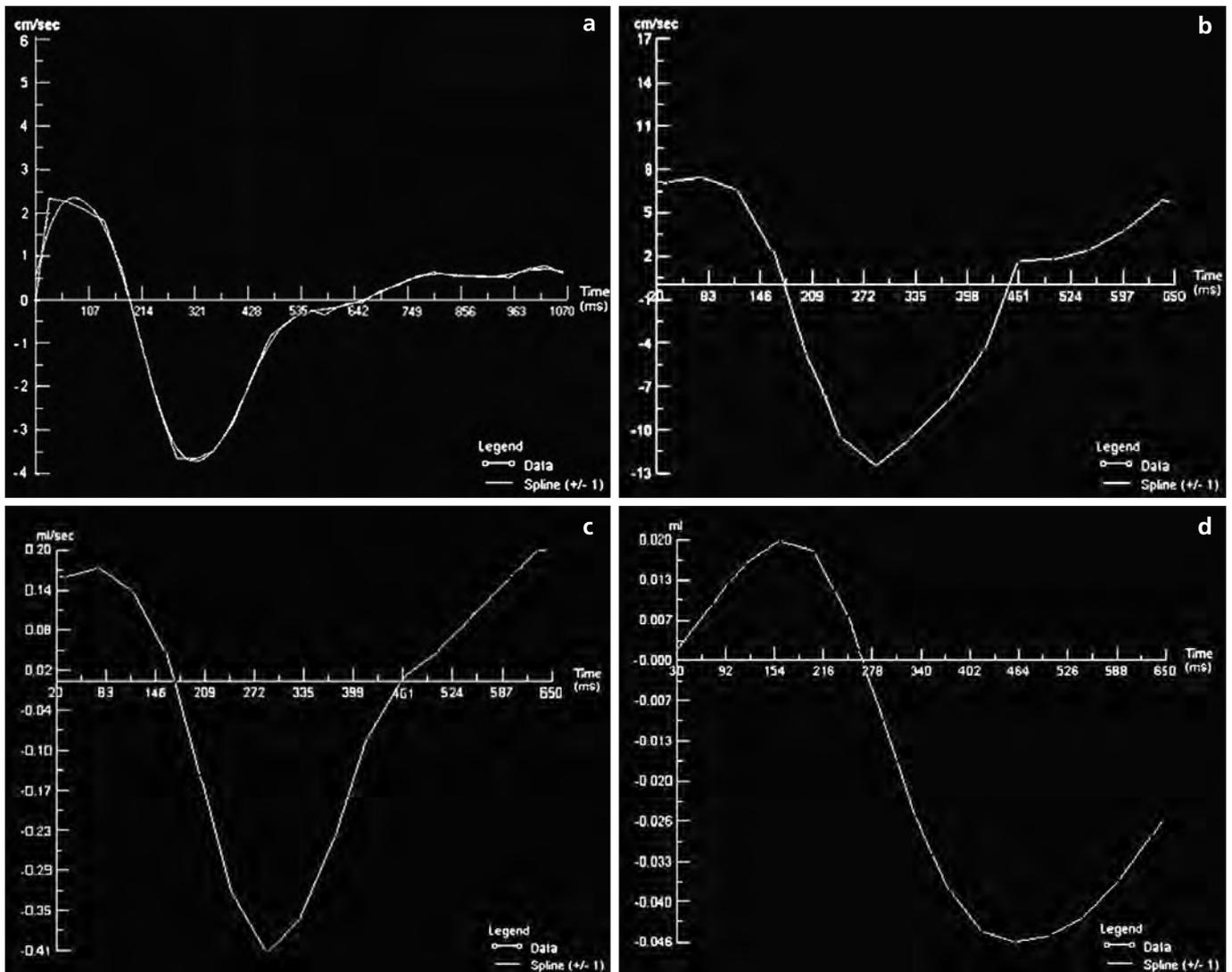
Figure. a–d. (a) Graphic showing aqueductal CSF velocity change with time in a single cardiac cycle. The area above tha baseline represents cranial velocity, while the area below the baseline represents caudal velocity. **(b)** Graphic showing aqueductal CSF peak velocity with time in a single cardiac cycle. **(c)** Graphic showing aqueductal CSF flow change with time in a single cardiac cycle. The area above the baseline represents cranial flow, while the area below the baseline represents caudal flow. **(d)** Graphic showing net aqueductal CSF flow in a single cardiac cycle. The curve in this graphic is different from the rest of the graphic curves; the end point of the curve gives the net flow value.

above the baseline represented cranial flow, while the area below the baseline showed caudal flow. Average velocity is shown by velocity-time graphic. The area above the baseline shows cranial and the area below the baseline represents caudal velocities. Peak velocity parameter is represented by peak velocity-time graphic. In the flow-time graphic, cranial flow is shown above the baseline while the caudal flow is shown below the baseline. Net flow is represented in net flow-time graphic. Net flow is extracted by integrating aqueductal area to the net volume.

For each individual, aqueductal area (mm^2); aqueductal peak flow velocity (cm/s); average flow rate (cm/s); average flow (L/min), calculated by average velocity × area of ROI); volumes in cranial and caudal directions (mL) in a cardiac cycle; and net volumes (mL), which are the sum of both amounts, were obtained quantitatively and with graphics.

Statistical analysis was performed using the SPSS statstical program. For double group comparison (between the group ≤14 years and other age groups), post hoc Mann-Whitney U test was used and for multiple group comparison, Kruskal-Wallis variance analysis was used. Multiple comparisons between sexes were performed by Student t test. Variable correlations (positive and negative correlations between age and flow parameters) were tested by Spearman rho rank test. Statistical significance was established at $P < 0.05$.

Results

For all patients aqueductal area was in a range of 1.2–4.8 mm^2 (mean, 2.6). Four of the cases had an aqueductal area less than 1.5 mm^2 (1.2 mm^2 being the lowest).

The mean flow parameter values were calculated with standard deviations (Table 1). While there was significant difference among age groups for peak velocity with Kruskal-Wallis variance analysis, there was no significant difference among other variables. On correlation study done by post-hoc Mann-Whitney U test, the peak velocity values in the 14 and younger group was found significantly higher than 15–24, 25–34, and 35–44 age groups ($P < 0.01$, $P < 0.05$, and $P < 0.01$, respectively). There was no significant difference between the peak velocity values of groups aged ≤14 years and ≥45 years. Although the average velocity, cranial, and net volume parameters were decreased, and average flow and caudal volume parameters were increased with age, the results were not statistically significant. While significant reverse-correlation between age and peak velocity was found ($P < 0.05$), no significant correlation was observed between age and other parameters. Also, without considering the age differences, there was no statistically significant difference between sexes (Table 2).

Discussion

Cine phase-contrast MRI has many advantages including non-invasiveness, no need for patient preparation or contrast media injection, no X-ray exposure, and an overall examination duration less than 15 min.

Today, although the high resolution imaging units are in use, there are still errors about velocity data. The reasons for the occurrence of these errors are reported as non-linearity of the gradients, eddy currents, partial volume effects, and error in ROI placement (5, 12, 13). In cases with narrow aqueducts, the error rate can increase due to difficulty in ROI placement (14). Reliable flow quantification is reported to be feasible if the diameter of the lumen is greater than 1.5 mm^2 (15). In our study, four cases had an aqueductal area less than 1.5 mm^2, 1.2 mm^2 being the lowest. However, these individuals did not have significant differences fom the rest of the cases concerning flow parameters. Mean aqueductal area values were between 2.01–3.10 mm^2 (mean, 2.67) according to age groups, whereas this value was between 1.2 and 4.8 mm^2 (mean, 2.35) independent of age. These results are consistent with the findings of studies in the literature (9, 16, 17). The comparison

Table 1. The mean flow parameter values (± standard deviation) according to age groups

	Peak velocity (cm/s)	Average velocity (cm/s)	Cranial volume (mL)	Caudal volume (mL)	Net volume (mL)	Aqueductal area (mm^2)
6–14 years (n = 15; 7F, 8M)	7.89 ± 2.57	−0.74 ± 0.55	0.016 ± 0.008	−0.026 ± 0.012	−0.010 ± 0.007	2.33
15–24 years (n = 9; 2F, 7M)	4.70 ± 1.61	−0.31 ± 0.16	0.013 ± 0.006	−0.019 ± 0.007	−0.005 ± 0.002	3.10
25–34 years (n = 12; 6F, 6M)	5.50 ± 2.89	−0.46 ± 0.48	0.014 ± 0.011	−0.023 ± 0.015	−0.007 ± 0.006	3.07
35–44 years (n = 11; 4F, 7M)	4.93 ± 1.83	−0.56 ± 0.25	0.012 ± 0.008	−0.021 ± 0.013	−0.009 ± 0.006	2.76
≥45 years (n = 13; 6F, 7M)	5.85 ± 1.80	−0.67 ± 0.26	0.010 ± 0.005	−0.020 ± 0.005	−0.009 ± 0.003	2.01
Total (n = 60; 25F, 35M)	5.95 ± 2.48	−0.57 ± 0.41	0.013 ± 0.008	−0.022 ± 0.011	−0.008 ± 0.005	2.67

F, female; M, male

Table 2. The mean flow parameter values (± standard deviation) of both sexes

	Peak velocity (cm/s)	Average velocity (cm/s)	Cranial volume (mL)	Caudal volume (mL)	Net volume (mL)
Male	6.35 ± 2.46	−0.52 ± 0.31	0.011 ± 0.009	−0.019 ± 0.010	−0.007 ± 0.004
Female	5.39 ± 2.44	−0.61 ± 0.47	0.015 ± 0.007	−0.023 ± 0.014	−0.010 ± 0.008

of aqueductal area among age groups yielded statistically significant results, but we do not consider this finding to be clinically important. Likewise, there were no statistically significant differences in the aqueductal area between sexes.

Velocity encoding (Venc) is the parameter showing sensitivity for the flow. The chosen Venc values show the maximal intraluminal flow velocity on the images. While a choice of Venc just over the maximum peak velocity increases accuracy, smaller chosen values will yield smaller results (14). Generally, the chosen Venc in aqueductal flow studies in the literature vary between 15 and 20 cm/s (10, 12, 15, 18). Based on our experience and reports in the literature we chose Venc as 20 cm/s. On the other hand, in patients who are predicted to have higher Venc, a higher value should be chosen. Cardiac gating can be achieved either prospectively or retrospectively. In our study we used prospective gating, which is the generally available form (12). The duration of prospective gating is longer than the retrospective form. The acquisition stops within about 200 ms of the next R wave for accurate detection of the next trigger. Thus the entire cardiac cycle (particularly the diastolic phase) is not evaluated. These are the disadvantages of prospective gating compared to the retrospective form.

Two changes in CSF circulatory physiology have been noted as part of aging: first, a trend towards lower CSF production, hence a decrease in CSF turnover; and second, greater resistance to CSF outflow (18, 19). Silverberg et al. suggest that if CSF production failure predominates, Alzheimer disease develops and if resistance to CSF outflow predominates, normal pressure hydrocephalus develops (19). On the other hand, Luetmer et al. found similar CSF flow rates in normal elderly patients, patients with Alzheimer disease, and patients with other forms of cognitive impairment (excluding normal pressure hydrocephalus), which suggests that flow rates are independent of cerebral atrophy (20). Slightly higher aqueductal CSF peak flow velocities and volume flow in both cranial and caudal directions were found in the group of elderly healthy volunteers, however, this was not statistically significant (5, 21). In various studies, aqueductal peak velocities are reported to show

great physiologic variations, independent of age (1.5–12.7 cm/s) (5, 8, 10, 14, 15). In our study, the peak velocities were found between 1.41 and 11.67 cm/s. For peak velocity, a statistically slight difference was found between ≤14 years age group and 15–24, 25–34, and 35–44 years age groups. There were no statistically significant differences among the other groups. Although, the age dependent nonsignificant results in flow parameters were in consistency with the studies in the literature (4, 5, 14, 18, 20), the only difference was the slight statistical difference between ≤14 years age group with the other groups.

Because there are few studies concerning adolescents, and these studies include small numbers of subjects, no comparison could be performed for this age group. In our study, we divided the individuals into five groups according to their ages including the adolescent age group ≤14 years. When the statistical difference between the adolescent group and the other age groups is taken into consideration, even though the difference is slight, we think that this difference should be considered in future clinical studies.

Different values have been reported in the literature for cranial, caudal and net volume parameters. Lee et al. (14), Brinkmann et al. (15), and Enzmann and Pelc (17) reported the following net volume results: 0.03 ± 0.01, 0.04 ± 0.02, and 0.06 ± 0.034 mL, respectively. As for cranial and caudal volumes, Schroeder et al. reported cranial values of 0.06 mL and caudal values 0.06–0.07 mL (10), while Barkhof et al. reported cranial values of 0.16 ± 0.10 mL and caudal values of 0.29 ± 0.19 mL (5). None of the above studies were performed with multiple age groups, and none included the adolescent age group. In our study, cranial, caudal, and net volume values were 0.002–0.034, 0.005–0.044, and 0.001–0.044 mL, respectively, independent of age. We think that these results represent normal physiologic variations.

In cine phase-contrast MR examination of aqueductal flow, average velocity, cranial and net volume parameters, average flow and caudal volume parameters of all age groups were not statistically significant. As for peak velocity, a statistically significant difference was found between age groups, which is consistent with other studies in the literature (22, 23). İskandar and

Haughton stated that peak CSF velocities vary significantly with age, and to determine the normalcy of a CSF flow measurement, it should be compared with age-appropriate normative data (22). Stoquart-ElSankari et al. concluded that CSF stroke volumes were significantly reduced in the elderly (23). In our study, there were no statistically significant differences among the other groups. Sex also had no statistically significant effect on flow parameters.

As a conclusion, in this study including a large number of cases, all of the peak velocities were within 1.41–11.67 cm/s range. As there were no meaningless high values, the values that are considerably larger than 11.67 should be used as clinicopathologic data in future studies. On the other hand, even though we have found net volume values in the 0.001–0.044 mL range independent of age, which seems quite wide, we think that values higher than 0.044 would be useful in future clinical studies.

References

1. Bradley WG Jr, Scalzo D, Nitz WN. Normal-pressure hydrocephalus: evaluation with cerebrospinal fluid flow measurements at MR imaging. Radiology 1996; 198:523–529.
2. Krauss JK, Regel JP, Vach W, Jüngling FD. Flow void of cerebrospinal fluid in idiopathic normal pressure hydrocephalus of the elderly: can it predict outcome after shunting? Neurosurgery 1997; 40:67–73.
3. Sherman JL, Citrin CM, Gangarosa RE, Bowen BJ. The MR appearance of CSF pulsations in the spinal canal. AJNR Am J Neuroradiol 1986; 7:879–884.
4. Jacobson EE, Fletcher DF, Morgan MK, Johnston IH. Fluid dynamics of the cerebral aqueduct. Pediatr Neurosurg 1996; 24:229–236.
5. Barkhof F, Kouwenhoven M, Scheltens P. Phase-contrast cine MR imaging of normal aqueductal CSF flow. Effect of aging and relation to CSF void on modulus MR. Acta Radiol 1994; 35:123–130.
6. Panigrahi M, Reddy BP, Reddy AK, Reddy JJ. CSF flow study in Chiari I malformation. Childs Nerv Syst 2004; 20:336–340.
7. Eguchi T, Taoka T, Nikaido Y, et al. Cine magnetic resonance imaging evaluation of communication between middle cranial fossa arachnoid cysts and cisterns. Neurol Med Chir 1996; 36:353–357.
8. Kim DS, Choi JU, Ryoong Huh R, Yun PH, Kim DI. Quantitative assessment of cerebrospinal fluid hydrodynamics using a phase-contrast cine MR image in hydrocephalus. Childs Nerv Syst 1999; 15:461–467.
9. Menick B. Phase-contrast magnetic resonance imaging of cerebrospinal fluid flow in the evaluation of patients with Chiari I malformation. Neurosurg Focus 2001; 11:E5.

10. Schroeder HW, Schweim C, Schweim KH, Gaab MR. Analysis of aqueductal cerebrospinal fluid flow after endoscopic aqueductoplasty by using cine phase-contrast magnetic resonance imaging. J Neurosurg 2000; 93:237–244.

11. Hoffmann KT, Lehmann TN, Baumann C, Felix R. CSF flow imaging in the management of third ventriculostomy with a reversed fast imaging with steady-state precession sequence. Eur Radiol 2003; 13:1432–1437.

12. Nitz WR, Bradley WG Jr, Watanabe AS, et al. Flow dynamics of cerebrospinal fluid: Assessment with phase-contrast velocity MR imaging performed with retrospective cardiac gating. Radiology 1992; 183:395–405.

13. Henry Feugeas M-C, Idy-Peretti I, Blanchet B, Hassine D, Zannoli G, Schouman-Claeys E. Temporal and spatial assessment of normal cerebrospinal fluid dynamics with MR imaging. Magn Reson Imaging 1993; 11:1107–1118.

14. Lee JH, Lee HK, Kim JK, Kim HJ, Park JK, Choi CG. CSF flow quantification of the cerebral aqueduct in normal volunteers using phase contrast cine MR imaging. Korean J Radiol 2004; 5:81–86.

15. Brinkmann G, Harlandt O, Muhle C, Brossmann J, Heller M. Quantification of fluid flow in magnetic resonance tomography: an experimental study of a flow model and liquid flow measurements in the cerebral aqueduct in volunteers. Rofo 2000; 172:1043–1051.

16. Gideon P, Thomsen C, Ståhlberg F, Henriksen O. Cerebrospinal fluid production and dynamics in normal aging: a MRI phase-mapping study. Acta Neurol Scand 1994; 89:362–366.

17. Enzmann DR, Pelc NJ. Cerebrospinal fluid flow measured by phase-contrast cine MR. AJNR Am J Neuroradiol 1993; 14:1301–1307.

18. Enzmann DR, Pelc NJ. Normal flow patterns of intracranial and cerebrospinal fluid defined with phase-contrast cine MR imaging. Radiology 1991; 178:467–474.

19. Silverberg GD, Mayo M, Saul T, Rubenstein E, McGuire D. Alzheimer's disease, normal pressure hydrocephalus, and senescent changes in CSF circulatory physiology: a hypothesis. Lancet Neurol 2003; 2:506–511.

20. Luetmer PH, Huston J, Friedman JA, et al. Measurement of cerebrospinal fluid flow at the cerebral aqueduct by use of phase-contrast magnetic resonance imaging: Technique validation and utility in diagnosing idiopathic normal pressure hydrocephalus. Neurosurgery 2002; 50:534–542.

21. May C, Kaye JA, Atack JR, Schapiro MB, Friedland RP, Rapoport SL. Cerebrospinal fluid production is reduced in healthy aging. Neurology 1990; 40:500–503.

22. İskandar BJ, Haughton V. Age-related variations in peak cerebrospinal fluid velocities in the foramen magnum. J Neurosurg 2005; 103:508–511.

23. Stoquart-ElSankari S, Balédent O, Gondry-Jouet C, Makki M, Godefroy O, Meyer ME. Aging effects on cerebral blood and cerebrospinal fluid flows. J Cereb Blood Flow Metab 2007; 27:1563–1572.