Unilateral versus bilateral deep brain stimulation

TO THE EDITOR: I read with great interest the article by Taba et al.1 (Taba HA, Wu SS, Foote KD, et al: A closer look at unilateral versus bilateral deep brain stimulation: results of the National Institutes of Health COMPARE cohort. Clinical article. J Neurosurg 113:1224–1229, December 2010). In that article 52 patients with advanced Parkinson disease (PD) were randomized to receive deep brain stimulation (DBS) to the subthalamic nucleus (STN) or the globus pallidus internus (GPI); complete data sets were available in 44 of the patients. All cases were started with unilateral implantation, and the patients were offered the choice of a contralateral implantation after 6 months based on inadequacy to address motor symptoms.

In the last sentence of the Results section, the following result was mentioned: “For each 1% increase in asymmetry in the baseline off-medication UPDRS [Unified Parkinson’s Disease Rating Motor Scale]–III score, the odds of receiving bilateral DBS decreased by a factor of 0.96.” That result is congruent with the data presented in Tables 3 and 4. It is also similar to the second sentence in the Conclusions: “There was a strong association between the degree of asymmetry in each patient’s PD and the preference for unilateral DBS.” However, those correct statements are contradicted in the Abstract. The last line in the Results section of the Abstract is “For every 1% increase in asymmetry, the odds of bilateral DBS increased by 0.96,” whereas I believe it meant to be “... decreased by 0.96.”

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Disclosure

The author reports no conflict of interest.

Reference


RESPONSE: Dr. Khaled has correctly pointed out that in our article there is a contradiction between text in the last sentence of the Results in the paper and the corresponding text in the Results section of the Abstract. The text in the Abstract is incorrect and should read “For every 1% increase in asymmetry, the odds of bilateral DBS decreased by 0.96.” The data contained in the Results and Conclusions in the paper are correct.

We thank Dr. Khaled for pointing out this error.

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Normal pressure hydrocephalus

TO THE EDITOR: I read with great interest the paper by Penn et al.8 (Penn RD, Basati S, Sweetman B, et al: Ventricle wall movements and cerebrospinal fluid flow in hydrocephalus. Clinical article. J Neurosurg 115:159–164, July 2011). As part of their study, the authors measured the CSF net flow rate through the aqueduct in 2 patients with normal pressure hydrocephalus (NPH) before and after shunt insertion and compared the findings with findings in 8 controls. I wish to discuss 2 topics of interest raised by the authors’ work: 1) Why is the amount of CSF exiting the ventricular system in the controls higher than the accepted CSF formation rate? 2) How is a high net flow of CSF into the ventricles in NPH sustained?

In their review of 4 of 6 MRI studies in which the CSF formation rate was elevated above accepted figures and found a range of between 1.5 and 3 times normal for this metric. Penn et al.8 quote a study by Kim et al.6 who found a net aqueduct stroke volume of 30.1 μl per cycle. Unfortunately, Kim et al. do not indicate the average heart rate in their study but to date no one has tried to explain the discrepancy.

The accepted CSF formation rate has been derived from CSF infusion studies and indicator dilution studies and is actually a measure of the amount of fluid leaving the cerebrospinal cavity principally via the arachnoid granulations but also by other accessory routes (the formation rate equals the absorption rate at steady state).
So in order for 1600 ml to be entering the basal cisterns per day, but only 500 ml leaving the arachnoid granulations per day, the cortex of the brain between these 2 sites would have to be absorbing 1100 ml per day. There is no pressure gradient between the subarachnoid space and the brain to sustain such an absorption rate, so an energy-utilizing pump would be required. Just such a pumping mechanism appears to exist. It has long been known that large molecules such as horseradish peroxidase will rapidly pass from the subarachnoid space into the perivascular spaces and then into the interstitial spaces of the brain. The arterial pulsations in the penetrating arterioles passing through the pial sheaths appear to drive CSF ahead of them through the perivascular spaces, not unlike the way a train entering a tunnel will push a column of air ahead of it. Simulated arterial pulsations induce fluid movements in the perivascular spaces of approximately 1 μl per heart beat. This would equate to about 80 ml per day per penetrating vessel, suggesting that perivascular absorption of 1100 ml/day is not out of the question. All that would then be required to explain the high aqueduct CSF flow would be for the CSF/interstitial brain fluid to make its way to the ventricle walls and then pass back into the ventricles. Thus, although only 500 ml/day of CSF would originate from the choroid plexus, with some of this fluid coming from the leakage of fluid from brain capillaries (10%–30%), about 1100 ml would be added from CSF recirculation through the interstitial spaces. Therefore, 1600 ml would leave the aqueduct per day. On the way through the subarachnoid space 1100 ml would be recirculated into the brain, with 500 ml continuing on to be reabsorbed over the vertex. Penn et al. accurately depict this physiology in their Fig. 3 (left) in which arrows pass from the subarachnoid space through the brain to the ventricles, but the mechanism of the brain absorption of CSF from the subarachnoid space is not discussed.

The second anomaly I wish to discuss is the finding of Penn et al. that in 2 cases of NPH the net aqueduct flow was reversed, averaging 7.2 ml/min or over 10 L per day. Other groups have found negative but much lower flows. Kim et al. noted a flow equating to approximately 5.4 L/day, and Balédent et al. noted a flow entering the ventricles of about 1.6 L/day in hydrocephalus. The measured absorption rate of CSF into the arachnoid granulations and accessory pathways is lower in NPH than in controls, at about 0.25 ml/min or 360 ml/day. Obviously if 10 L/day is leaving the subarachnoid space via the aqueduct, 360 ml/day is exiting via the arachnoid granulations, and there is no net flow from the choroid plexus through the aqueduct to replenish the subarachnoid space; then in the absence of another source of fluid, the subarachnoid space will be completely depleted. Penn et al. get around this problem in their model by suggesting that most of the excess CSF entering the ventricles passes into the brain, through the parenchyma, and exits the brain surface back into the subarachnoid space (see Fig. 2 right). This is the mirror image of the normal findings in Fig. 3 left. The problem is that again there is no pressure gradient from ventricle to subarachnoid space to propel the fluid, but in addition there is no obvious energy-utilizing pump available to do this either (unlike the perivascular pump, which goes the other way). The flow out of the cortex would have to be swamping the perivascular flow in. The perivascular flow theoretically continues to occur into the brain even against a pressure gradient. The only solution available to the problem is for the cerebral cortex to become a net producer of CSF and the subependymal white matter to become a net absorber of CSF with little fluid passing across the parenchyma.

As previously noted, the cortex is a small net producer of CSF (10%–30%). According to Starling’s laws, interstitial fluid exits the arteriolar side of the capillary bed because the hydrostatic pressure exceeds the oncotic pressure and returns on the venular side because the oncotic pressure exceeds the hydrostatic pressure. As the flows do not match exactly, a small net outflow of interstitial fluid adds to the CSF volume. In order for the cortex to produce up to 10 L per day, the venous pressure would need to be elevated above the interstitial pressure, and for the deep white matter to be a net absorber of 10 L/day, the venous pressure would need to be lower than the ventricular pressure. I have studied NPH for over 10 years using MRI to measure differential blood flow from the deep and superficial venous territories in the brain and have noted discrepancies entirely consistent with the suggestion that the superficial veins increase in pressure in NPH but the deep veins remain unchanged. Thus, unless a pump from the ventricle to cortex can be found in NPH, Penn et al.’s findings of reversal of flow in the aqueduct in NPH provide additional evidence that the real underlying physiology of NPH is altered venous pressure in the superficial brain.

Finally, Penn et al. noted that the CSF dynamics returned to normal after shunt insertion, indicating that not all of the ventricular CSF exits via the shunt. Therefore, the CSF absorption abnormalities may be reversible. I have noted similar findings; shunting NPH patients increases sagittal sinus blood flow and would be consistent with a reduction in venous pressure and a reversal of the abnormal physiology. Thus, I believe that explaining the anomalies noted in the CSF outflow in the paper of Penn et al. appears to be important in understanding both the normal physiology of CSF flow and the physiology of NPH.

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