Cerebral venous thrombosis and isolated intracranial hypertension without papilledema in CDH

To the Editor: I wish to thank Quattrone et al.¹ for their engaging article on chronic daily headache (CDH) and cerebral venous thrombosis (CVT).¹ Their finding that almost 10% of the population with CDH have evidence of CVT is remarkable. However, I do have concerns over the exclusive reliance on MR venography (MRV). In my experience, the area of transverse sinuses (TS) that is indicated on the MR venograms in the article is highly variable, with narrowing, especially when bilateral, not necessarily indicative of venous thrombosis. In other examples presented, the area of abnormality is quite focal, leaving one to wonder why the clot has not extended to involve a larger area of the vessel. It would have been interesting if conventional venography had been included to corroborate the findings. Finally, I will be eagerly anticipating a therapeutic trial of the subset of patients with CDH and CVT.

Abraham Totah, MD, *Clearwater, FL*

Reply from the Authors: We appreciate Dr. Totah's interest in our article,¹ in which we describe the occurrence of CVT in subjects with CDH. Dr. Totah raises some issues on the reliability of MRV in detecting CVT. MRV is the method of choice for the diagnosis of CVT because it is a noninvasive technique that can demonstrate the absence of flow in the thrombosed sinus or the frayed appearance of a thrombosed sinus that had subsequently recanalized.^{2,3} However, there are pitfalls of this technique that may, in doubtful cases, make cerebral angiography necessary. We agree with Dr. Totah that flowing abnormalities of TS not related to vein thrombosis, especially when unilateral, may occasionally be observed on MRV in normal subjects. A common problem is the lack of flow in the proximal portion of TS due to hypoplasia of the sinus, a normal variant that can simulate thrombosis on MRV.^{2,4} In contrast, we disagree with Dr. Totah regarding the significance

of the bilateral flowing abnormalities of TS. Indeed, a recent MRV study showed that flow gaps in the dominant TS were never observed in healthy subjects, indicating that involvement of both TS rarely occurs in normal individuals, and should be considered a pathologic condition.⁵ In accordance with these data, we demonstrated in our article¹ that only five of 114 subjects with CDH had flowing abnormalities in both TS. It is noteworthy that four of these five subjects had isolated intracranial hypertension, a condition that is known to be associated with CVT. Our findings strongly indicate that flow gaps in the distal portion of both TS are highly suggestive of venous thrombosis, which can lead to intracranial hypertension (with or without papilledema). On this basis, we maintain that subjects who present with CDH showing bilateral flowing abnormalities in the distal portion of TS should undergo lumbar puncture to exclude isolated intracranial hypertension. Finally, we agree with Dr. Totah that a therapeutic trial should be considered in such patients.

A. Quattrone, MD, F. Bono, MD, K. Pardatscher, MD, *Catanzaro, Italy*

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References

1. Quattrone A, Bono F, Oliveri RL, et al. Cerebral venous thrombosis and isolated intracranial hypertension without papilledema in CDH. *Neurology* 2001;57:31–36.
2. Perl J, Turski PA, Masaryk TJ. MR angiography. Techniques and clinical applications. In: Scott W, ed. *Magnetic resonance imaging of the brain and the spine*. 2nd ed. Philadelphia: Lippincott-Raven, 1996:1547–1618.
3. Boussier MG, Russell RR. *Cerebral venous thrombosis*. London: Saunders, 1997.
4. Mas JL, Meder JF, Meary E, et al. Magnetic resonance imaging in lateral sinus hypoplasia and thrombosis. *Stroke* 1990;21:1350–1356.
5. Ayanzen RH, Bird CR, Keller PJ, et al. Cerebral MR venography: normal anatomy and potential diagnostic pitfalls. *AJNR Am J Neuroradiol* 2000; 21:74–78.

Preservation of golf skills in a case of severe left lobar frontotemporal degeneration

To the Editor: I was interested and amused by the article by Venneri and Shanks¹ on preservation of golf skills despite a large left frontotemporal brain lesion. I assume the patient was right-handed. The article brought to mind the following observation. In contrast to sporting activities that require only one hand, such as using a tennis racket, the preference for swinging a golf club (or baseball bat, for that matter) in left-handers may be either left or right. However, I am not aware of any right-handed person who has expressed a desire to swing a golf club left-handed. Could the natural swing preference relate to cerebral language dominance, which in left-handers can be either left hemisphere in 70% or atypical (right hemisphere or bilateral) in 30%, assuming no early brain injury?² This compares to only 4 to 6% of right-handers who have atypical language dominance, usually bilateral.³

Richard S. McLachlan, MD, *Abu Dhabi, United Arab Emirates*

Reply from the Authors: We thank Dr. McLachlan for his interest in our article¹ and for his comments about hand preference and sporting activities. We can confirm that our patient was right-handed, had a right club swinging preference, and his profound progressive dysphasia with pronounced left frontotemporal atrophy supported left language lateralization. Dr. McLachlan observed that in sports that require the use of one hand, like tennis, handedness seems to respect cerebral language dominance. He also speculated that this might be less exclusively the case with bimanual sports such as golf. Our reading of the factor analytic

literature on side bias for manual activities, including sports, suggested that hand use patterns in bimanual activities (like swinging an axe or using a bat) may load onto factors additional to those that have been related to unimanual tasks such as handwriting.⁴ This research showed a marked increase in nondominant hand use in both right-handers (10% increase) and left-handers (26% increase) for bimanual skills. These results have been confirmed by another study.⁵ Therefore, it is possible that bimanual activities are more plastic than unimanual skilled tasks in the sense that they may be developed more flexibly and may be less constrained by hemispheric lateralization, including lateralization for language.

Annalena Venneri, PhD, Michael F. Shanks, FRCPsych DPhil, David P. Carey, PhD, *Aberdeen, UK*

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References

1. Venneri A, Shanks MF. Preservation of golf skills in a case of severe left lobar frontotemporal degeneration. *Neurology* 2001;57:521–524.
2. Rasmussen T, Milner B. The role of early left-brain injury in determining lateralization of cerebral speech functions. *Ann NY Acad Sci* 1977; 299:355–369.
3. Springer JA, Binder JR, Hammeke TA, et al. Language dominance in neurologically normal and epilepsy subjects: a functional MRI study. *Brain* 1999;122:2033–2046.
4. Steenhuis RE, Bryden MP. Different dimensions of hand preference that relate to skilled and unskilled activities. *Cortex* 1989;25:289–304.
5. Steenhuis RE, Bryden MP, Schwartz M, Lawson S. Reliability of hand preference items and factors. *J Clin Exp Neuropsychol* 1990;12:921–930.

Reversible parkinsonism and MRI diffusion abnormalities in cortical venous thrombosis

To the Editor: We read with interest the recent published article by Jenkins et al.¹ The authors report an interesting and well-documented patient with reversible parkinsonism due to deep venous system (incidentally, the title wrongly reports cortical venous thrombosis). MR diffusion-weighted images (DWI) demonstrated reversible hyperintensities in basal ganglia. The authors speculate that the reversible cellular swelling due to the increased venous pressure restricts water motion; this would lead to a reversible alteration of the diffusion without producing irreversible neuronal damage. In effect, diffusion hyperintensities partially disappeared at follow-up. Although this hypothesis is interesting, alternative explanations are possible.

Contributions other than restricted diffusion may account for the hyperintensity on DWI. In particular, residual T2 contrast may variously contribute (T2 shine-through effect). The only way to quantify the diffusion alterations separating the contribution of the T2 shine-through effect is to calculate the apparent diffusion coefficient (ADC).²

Various conditions with increased extracellular water content but almost complete sparing of the neurons, such as venous edema, may be evident on DWI as hypointense or mildly hyperintense lesions.³ In all these conditions, the diffusion is expected to be increased and not reduced, owing to the prevalent extracellular edema. The more- or less-intense signal on DWI depends on the opposite contribution of the T2 shine-through effect and of the increased diffusion. ADC calculation precisely defines the alteration of the diffusion and identifies among hyperintense lesions those with restricted diffusion (nonreversible neuronal damage) from those with increased diffusion (reversible extracellular edema).

A restricted diffusion of an ischemic parenchyma usually indicates an irreversible damage of the tissue,⁴ and on DWI corresponds to a strongly hyperintense region, similar to the lesions of the right thalamus and the splenium reported in the authors' patient.¹ On the contrary, a mild hyperintensity may be simply due to a T2 shine-through effect, similar to the lesions of the left basal ganglia of this patient. In effect, at follow-up the more hyperintense lesions did not disappear, suggesting the presence of irreversible neuronal damage, different from the less hyperintense lesions. Similar findings were reported in another recently published article.⁵

ADC calculation would have distinguished between regions with restricted and regions with increased diffusion, and would have identified the neuronal damage among the extracellular edema.

M. Bergui, MD, G.B. Bradic, MD, *Turin, Italy*

Reply from the Authors: Bergui and Bradic are indeed correct that the title should have read deep cerebral venous thrombosis. This may be owing in part to the fact that this article was originally significantly longer, and was abbreviated at the request of the journal. In fact, the original working title was "Reversible parkinsonism and MRI diffusion abnormalities in cerebral venous thrombosis."

With regard to the ADC mapping, the authors are correct—this is the most reliable way of demonstrating truly restricted

water motion; however, omitted from the imaging because of space constraints were T2-weighted images; the first one showed little T2 abnormality, and the second more T2 abnormality, which should have produced more T2 shine-through on the second imaging series. T2* gradient echo imaging through the brain did not show any blood/susceptibility changes to explain the changes in diffusion signal based on susceptibility effects. We did not perform multiple B-value-diffusion imaging—only two B values were used, B = 0 and B = 1000—making ADC mapping potentially less accurate. Additionally, owing to funding constraints here in Canada, we do not have the required software for ADC mapping in our unit. Although earlier articles on restricted ADC (and diffusion tensor hyperintensity) did show that the changes were usually irreversible, recent work with recombinant tissue-type plasminogen activator and imaging after its administration has shown that restricted ADC and diffusion tensor hyperintensity may be reversible in acute ischemia and thus it is quite conceivable that venous "diffusion hyperintensity" could reverse too, especially given the mechanism of production of the venous ischemia.

Another recently published article,⁷ which was also omitted from our references because of space limitations, described three types of abnormality associated with venous thrombosis in which ADC was measured, one of which was decreased ADC and trace image hyperintensity, which they felt was related to irreversible tissue injury. It was also noted, however, that even areas of reduced ADC in venous thrombosis, in comparison with areas of reduced ADC in arterial stroke, had a much better prognosis in terms of tissue damage finally visualized. They postulated that this was because cellular swelling in venous thrombosis allows some perfusion to occur, at lower flat rates. Therefore, the cell would not be irreversibly damaged. This compares to arterial occlusion, in which no flow occurs into the cell swollen by cytotoxic edema, with irreversible damage as a result.

M. Jenkins, N. Hussain, D. Lee, M.S. Jog, MD, FRCP, *London, Ontario, Canada*

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References

1. Jenkins M, Hussain N, Lee D, Jog MS. Reversible parkinsonism and MRI diffusion abnormalities in cortical venous thrombosis. *Neurology* 2001;57:364–366.
2. Schaefer PW, Grant PE, Gonzalez RG. Diffusion-weighted MR imaging of the brain. *Radiology* 2000;217:331–345.
3. Corvol JC, Oppenheim C, Manai R, et al. Diffusion-weighted magnetic resonance imaging in a case of cerebral venous thrombosis. *Stroke* 1988; 29:2649–2652.
4. Moseley ME, Kucharczyk J, Mintorovitch J, et al. Diffusion-weighted MR imaging of acute stroke: correlation with TW-weighted and magnetic susceptibility-enhanced MR imaging in cats. *Am J Neuroradiol* 1990;11: 423–429.
5. Forbes KP, Pipe JG, Heiserman JE. Evidence for cytotoxic edema in the pathogenesis of cerebral venous infarction. *Am J Neuroradiol* 2001;22: 450–455.
6. Kidwell CS, Sauer JL, Mattiello J, et al. Thrombolytic reversal of acute human cerebral ischemic injury shown by diffusion/perfusion magnetic resonance imaging. *Ann Neurol* 2000;47:467–469.
7. Ducreux D, Oppenheim C, Vandamme X, Dormont D. Diffusion-weighted imaging patterns of brain damage associated with cerebral venous thrombosis. *Am J Neuroradiol* 2001;22:261–268.

Anomalous anatomy of speech-language areas in adults with persistent developmental stuttering

To the Editor: I read with interest the article by Foundas et al.,¹ which is the latest in a line of neurologic reports that confuse the cause and effect of stuttering (stammering). The observations associated with this clinical problem of chronic involuntary blockage are not disputed. That these observations can be interpreted as a cause of blockage is neurologically impossible.

Because unintended blockage of speech is an aberration of normal speech processing, which is a manifestation of synchronization of phonation (for speech power) with articulation (that shapes phonatory power into the sounds of speech), the essence of fluent speech is the timing of speech sound phonatory/articulatory synchronization.

Any cause of blockage has to account for why it can be involun-

tary (otherwise it would never become chronic), and, more to the point, how high-speed speech sounds can be produced with low-speed, cognitive/linguistic equipment.

Synchronization speed is revealed by the syllable rate (no sound can be produced outside the context of a syllable) multiplied by the number of sounds per syllable. Syllable and cognitive thinking rates turn out to be roughly the same, which is fortunate, otherwise we would be unable to speak at the same rates we think. Decades ago, George Miller demonstrated the cognitive rate to be 7 ± 2 per second.²

In 1964, I inadvertently discovered that this is also the syllable rate, when I found that voluntary fluency prevented stammering when each sound is under voluntary control. Unfortunately for treatment, each sound had to be a syllable unto itself, which resulted in a speech rate so slow that it droned.³

Natural speech consists of syllables with up to six or more

sounds per syllable. Thus, sounds in the word “sounds” are synchronized at about 25 to 45 per second (7 ± 2 syllables per second $\times 5$ articulatory adjustments per five-sound syllable).

In 1965, Stromsta⁴ defined stammering as a static involuntary articulatory posture that blocks fluent overlapping coarticulatory transitions. This definition was confirmed by being the basis of predictions of recovery for 63 2- to 4-year-olds suspected of early stammering. The outcomes were verified 10 years later: every child who showed the defining signs of stammering had developed chronic stammering; the others spoke normally.

The reason the Tulane study cannot have causal implications for stammering is because the enlarged linguistic areas of Broca and Wernicke are intimately related to the slow cognitive function rates Miller described and are readily available to voluntary control, which disqualifies them as a cause of involuntary blockage. Wernicke's area is for speech perception and Broca's area is for speech planning. Aside from the fact that neither can operate at rates even close to speech synchronization rates, Wernicke's area is far too slow to have any role in the timing of high-speed speech. Broca's area, though it provides the specifications for speech-sound production, is likewise too slow to have any role in the timing of high-speed phonatory/articulatory synchronization. It is when timing is awry that stammering occurs. Thus, the investigators postulate “that anomalous cerebral dominance, reflected by anomalous cortical anatomy in various regions, may put an individual at increased risk for the development of stuttering” (stammering); however, they report a consequence of chronic stammering, not a cause. It should be noted that Lee Edward Travis, the primary author of the cerebral dominance theory, tested and rejected it in the mid-1930s as a cause of stammering (Travis, personal communication).

Complex as this letter may seem, it merely scratches the surface of normal speech production, let alone stammering and its causes. The Tulane study and other similar studies that attempt, by implication, to suggest an underlying cerebral disorder as a basis of stammering are contradicted by how the neural mechanism of speech is organized. The cerebrum has nothing to do with high-speed speech timing.

William H. Perkins, MD, *Los Angeles, CA*

Reply from the Editor: Briefly, Dr. Perkins contends that the cerebrum, especially Broca's and Wernicke's areas, is cognitively and linguistically too slow to process high-speed speech sounds. He mistakenly presumes that cerebral processing for speech is purely sequential and, if he is willing to accept the importance of subcortical and cerebellar mechanisms in the control of phonation/articulation, overlooks their important cortical connections.⁵⁻⁷

Miller's thesis of the magic number 7 involves paradigms of memory, not solely the mode of thinking.² Believing that “syllable and cognitive thinking rates turn out to be roughly the same . . .” would mean that we think no faster than we talk, which has absolutely no basis in neuropsychology.⁵⁻⁷

We do not “select” the sounds within our sentences from the larynx or other nonbrain structures, any more than our gall bladder tells us what food to buy or our kidney chooses our beverage. Whether the selection and control of our sound output resides in our cortical or subcortical networks, negating cerebral influence leaves what alternative?⁵⁻⁷

Simply put, when speaking, the message-to-be-communicated develops in stages and the output of one stage provides input to the other; planning and programming of speech in chunk-sized units precedes their actual production, making it likely that low-speed cognitive/linguistic equipment can indeed produce high-speed speech sounds. There is evidence (within the brain) for a rhetorical/semantic/syntactic system, which controls lexico-syntactic structures, as well as a phonologic/phonetic system, which generates articulatory shapes. Both systems, whose functions temporally overlap, can access the mental lexicon. The former system can also access relevant memories, and the latter can access the mental syllabary.^{6,8}

Further, recent data focus on left inferior frontal cortex and right motor/premotor cortex as relevant in merging linguistic and affective prosody in speech-motor output, a system possibly disrupted in stutterers.⁹

Scientific inquiry focuses on testable hypotheses with alternative models. Seemingly, Dr. Perkins does not dispute the data of Foundas et al.¹ Therefore, what is the significance of their findings? True, the cortical aberrations they elegantly describe may not be causal to stuttering—they could result from stuttering behaviors or could be epiphenomena. Regardless, the authors do not infer direct causality, but rather contend that anomalous anatomy is a risk factor for the development of stuttering.

The lack of a genuine nosology for stuttering has obfuscated our attempts to find the etiology for this malady. Unfortunately, the area of speech pathology includes many ailments in which the symptom, sign, and disease process are interchangeable and isomorphic (i.e., one has the symptom of stuttering, the sign of stuttering, and is diagnosed as a stutterer). Imagine if that were the standard approach to back pain or coma!

The data of Foundas et al.¹ provide a possible nosology for stuttering. Such information can sequester different stutterers based on shared/different anomalous cortical structures, recognizing inputs and outputs to subcortical systems, and points the way for future novel genetic, imaging, clinical, and therapeutic approaches.

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References

1. Foundas AL, Bollich AM, Corey DM, Hurley M, Heilmann KM. Anomalous anatomy of speech-language areas in adults with persistent developmental stuttering. *Neurology* 2001;57:207–215.
2. Miller G. *The psychology of communication*. New York: Basic Books, 1967.
3. Perkins WH. *Neural mechanisms of stammering*. Reno, NV: Athens Press (in press).
4. Stromsta C. *Elements of stuttering*. Oshtemo, MI: Atsmorts Publishing, 1986.
5. Kandel ER, Schwartz JH, Jessell TM. *Principles of neural science*. New York: McGraw Hill, 2000:1169–1187.
6. Indefrey P, Levelt WJM. The neural correlates of language production. In: Gazzaniga MS, ed. *The new cognitive neurosciences*. Cambridge, MA: MIT Press, 2000:845–865.
7. Mesulam MM. *Principles of behavioral and cognitive neurology*. New York: Oxford, 2000.
8. Levelt WJM. *Speaking: from intention to articulation*. Cambridge, MA: MIT Press, 1989.
9. Salmelin R, Schnitzler F, Schmitz F, Freund HJ. Single word reading in developmental stutters and fluent speakers. *Brain* 2000;123:1184–1202.

Randomized pilot trial of β INF1a (Avonex) in patients with inclusion body myositis

In the article, “Randomized pilot trial of β INF1a (Avonex) in patients with inclusion body myositis” by The Muscle Study Group (Neurology 2001;57:1566–1570), there was a factual error. In the background section of this article, the prevalence of inclusion body myositis (IBM) was misquoted. An erroneous prevalence of 4 to 9/100,000 was reported based on the study by Phillips et al. (reference 1 in the original article). The actual prevalence figures reported in that study were 4 to 9/1,000,000. The authors apologize for the error.

Miller Fisher syndrome: MRI findings

In the NeuroImage, “Miller Fisher syndrome: MRI findings” by Garcia–Rivera et al. (Neurology 2001;57:1755), the name of one of the authors was inadvertently omitted. T.D. Rozen, MD, should be the second author listed. The publisher apologizes for this error.

Normal plasma levels of orexin A (hypocretin 1) in narcoleptic patients

In the article, “Normal plasma levels of orexin A (hypocretin 1) in narcoleptic patients” by Dalal et al. (Neurology 2001;56:1749–1751), there was a calculation error. The plasma levels of orexin A depicted in figure 1B and reported in the text are tenfold too high due to a calculation error related to the extraction procedure applied to the plasma. The values reported for CSF, which was not extracted, are correct. Therefore, orexin A levels in healthy volunteers are about 15 times higher in CSF as compared with plasma. The authors apologize for this error.

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