# MR perfusion imaging reveals regions of hypoperfusion associated with aphasia and neglect

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**Article abstract**—*Objective:* To evaluate diffusion-weighted imaging (DWI) and MR perfusion imaging (MRPI) as tools for identifying regions of infarct and hypoperfusion associated with aphasia and neglect in hyperacute stroke. Secondary goal: to establish a functional correlate of a radiologically defined "ischemic penumbra." *Methods:* Forty subjects underwent DWI, MRPI, and standardized tests for lexical deficits or hemispatial neglect within 24 hours of stroke onset or progression. Ten patients had repeat DWI, MRPI, and cognitive testing after 3 days (in some cases after reperfusion therapy). Pearson correlations between error rate on cognitive testing and volume of abnormality on DWI versus MRPI were determined at each time period, and regions of hypoperfusion corresponding to specific cognitive deficits were identified. *Results:* Error rate was more strongly correlated with volume of hypoperfused tissue on MRPI (r = 0.65 to 0.93; p < 0.01 to p < 0.0003) than with volume of lesion on DWI (r = 0.54 to 0.75; p = 0.14 to p < 0.01) for dominant and nondominant hemisphere stroke, at each time point. Forty-eight percent of aphasic patients and 67% of those with hemispatial neglect had either no infarct or only small subcortical infarct on DWI, but had focal cortical hypoperfusion. Patients who had successful reperfusion therapy showed resolution of the hypoperfused territory beyond the infarction on repeat MRPI and showed resolution of corresponding deficits. *Conclusions:* MRPI shows regions of hypoperfused cortex associated with lexical deficits or hemispatial neglect, even when DWI shows no infarct or only small subcortical infarct. MRPI–DWI mismatch indicates regions of functionally salvageable tissue.

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Traditional teaching in neurology about brainbehavior relationships was based on associations between structural lesions (typically stroke) and chronic deficits in selected patients whose deficits persist 3 months or more after brain injury. This approach may introduce a selection bias, in that it excludes patients who recover in the first few months, even if they have a substantial lesion in an investigated territory. Another limitation of lesion-deficit studies in chronic stroke is that there is substantial reorganization of structure-function relationships during the first few days to weeks after brain injury.<sup>1,2</sup> Therefore, the original structure–function relationships may not be discernible in patients with chronic lesions. To circumvent these problems, more recent investigations of lesion-deficit associations focus on impairments that arise at the time of brain injury. For example, cortical stimulation studies identify impairments that result from "temporary lesions" created either by direct stimulation of the cortex during surgery,3 or by stimulating implanted subdural electrodes placed to map crucial functions prior to surgery.<sup>4</sup> Because the areas stimulated during these studies are generally in and around regions of cortex being considered for resection for either a seizure focus or structural lesion, these areas may have already undergone some degree of functional reorganization.

For these reasons, lesion-deficit correlations would be best identified in premorbid, normal individuals at the onset of brain dysfunction, prior to the opportunity for reorganization. A potential source of such data is the study of impairments in acute stroke. However, hypoperfused regions surrounding the acute infarct are likely to contribute to the behavioral manifestations.<sup>5</sup> It is now possible to image the entire region of both densely ischemic tissue and hypoperfused tissue at the very onset of stroke (<24hours), through the newly developed techniques of diffusion-weighted imaging (DWI) and MR perfusion imaging (MRPI). DWI shows areas of brain where there is decreased diffusion of water due to cytotoxic edema; it is highly sensitive at discerning densely ischemic tissue within the first few hours of stroke

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onset. MRPI reveals regions of tissue that are currently hypoperfused, and may be dysfunctional.

In this paper, we evaluated the hypothesis that the severity of cognitive impairment (hemispatial neglect or aphasia) in hyperacute stroke correlates more strongly with the volume of abnormality on MRPI than with the volume of abnormality on DWI. We also examined the hypothesis that patients with "cortical" deficits such as aphasia and hemispatial neglect who have only subcortical lesions (on DWI) have regions of cortical hypoperfusion (on MRPI) that can account for their clinical findings. We documented not only impaired functions associated with the hypoperfused tissue, but also resolution of the deficit with reperfusion of that brain region. In these cases, reperfusion was achieved with pharmacologic elevation of blood pressure, or with urgent endarterectomy, because the patients were not candidates for thrombolytic therapy or angioplasty or stenting. The findings support the proposal that the MRPI abnormality minus the DWI abnormality (the "diffusion-perfusion mismatch") represents functionally salvageable tissue, or "the ischemic penumbra."6,7 Previous reports have not quantified functional recovery due to reperfusion of the penumbra with detailed behavioral testing before and after intervention.

The objectives this investigation were to 1) evaluate DWI and MRPI as tools for identifying regions of dense ischemia and hypoperfusion associated with aphasia and neglect in hyperacute stroke (<24 hours from onset of symptoms or progression) and 2) establish a functional correlate of a radiologically defined ischemic penumbra, and illustrate how such data confirm the crucial role of circumscribed areas of the brain for particular cognitive functions.

Methods. Subjects. All patients with the clinical diagnosis of acute, unilateral hemispheric stroke who presented to Johns Hopkins Hospital within 24 hours of symptom onset or symptom progression were considered for inclusion. Additional inclusion criteria were 1) ability to give informed consent or to indicate a family member able to give informed consent and 2) premorbid proficiency in English. Exclusion criteria included 1) need for intubation or ongoing IV sedation, 2) severe claustrophobia, 3) hemorrhage on initial CT, 4) cardiac pacemaker or ferromagnetic implants, and 5) pregnancy. Each patient underwent cognitive testing, MRPI, DWI, and conventional MRI <24 hours from onset or stroke progression. A subset of patients had repeat DWI, MRPI, T2-weighted MRI, and cognitive testing 3 days after the initial tests (in some cases after reperfusion therapy), in order to evaluate the concept of an ischemic penumbra and to assess the role of the reperfused regions in cognitive functions impaired by the stroke. All patients or their identified decision makers gave informed consent for the study, as approved by the Joint Commission on Clinical Investigation of Johns Hopkins Medical Institutions.

*Cognitive tests.* The goal of cognitive testing was to identify functions that were clearly impaired compared with expected premorbid function in a short bedside visit, rather than to comprehensively assess neuropsychological

functioning or to identify strengths or weakness that vary across normal subjects. Therefore, the battery for dominant hemisphere stroke was limited to single word tasks, and the battery for nondominant stroke was limited to tests for hemispatial neglect. Scores were converted to a total percent incorrect (total errors/maximum score  $\times$  100). The majority of patients in this study were tested in the emergency department or in radiology while they awaited MRI studies.

Patients with dominant hemisphere stroke were given a bedside battery to evaluate the various levels of representations and processes underlying lexical tasks such as auditory and reading comprehension, picture naming, tactile naming, oral reading, and repetition. The tests included 1) oral and written naming of pictured objects (n = 34); 2) oral naming of objects with tactile input (n = 17); 3) oral reading of words (n = 34) and "pseudowords" (n = 25); 4) spelling to dictation of words (n = 34) and pseudowords (n = 25); 5) spoken word-picture verification (n = 34);6) written word-picture verification; and 7) repetition of words (n = 34) and pseudowords (n = 25). For wordpicture verification tasks, the set of pictures was presented three times: once with the corresponding word (e.g., a pictured cup with the word "cup"), once with a semantic foil (e.g., cup with the word "plate"), and once with a visually or phonologically related foil (e.g., cup with "cut"). The patient had to respond "yes" or "no" to verify or deny the correspondence between the picture and the word. Additionally, prior to responding in oral reading and dictation tasks, subjects were asked to discriminate words versus pseudowords (make a "lexical decision"). Word and object stimuli were matched across tasks for semantic category, familiarity, frequency, grammatical word class, and length. Liberal scoring of pseudoword spelling and pronunciation were used. Patients who had repeat testing were administered alternative forms of the battery with identical tasks but different stimuli matched for word length. frequency, and grammatical word class. Standardization of this battery was previously described.8 Normal elderly subjects scored close to 100% (all scored above 90%).

Patients with nondominant hemisphere stroke were given a battery of bedside tests to evaluate for hemispatial neglect at various levels of spatial representation. Tests included the following. 1) Oral reading and spelling of lists of frequency- and length-matched words and pseudowords (e.g., "samp") in standard print, mirror-reversed print, and vertical print (as reported elsewhere<sup>9</sup>). 2) Perceptual tasks in three spatial locations (directly in front, 45° to the subject's left, and 45° to the subject's right), in which 30 circles and 30 circles embedded in squares were presented, 20 with gap on the left side, 20 with a gap on the right, and 20 with no gap; patients reported "gap" or "no gap." 10 3) Perceptual-motor tasks of line cancellation; the Bells test;<sup>11</sup> and copying the "Ogden scene" (a house, a fence, and two trees), once with the scene right side up and once with the scene rotated 180°. 4) Motor tasks to test motor extinction, in which patients without hemiplegia were asked to click a golf counter with each hand as quickly as possible for 1 minute<sup>12</sup> in three conditions: each hand independently, simultaneously with the hands at the subject's sides, and simultaneously with arms crossed across the chest (to distinguish impaired clicking with the left hand versus impaired clicking on the left side of the body).

Imaging. The MR protocol included MRPI. DWI. and conventional MRI (sagittal T1-weighted; axial, fast spinecho T2-weighted; axial fluid attenuated inversion recovery [FLAIR] sequences; and MR angiography). Scans were obtained on a 1.5-tesla, echo planar imaging (EPI) capable system (Signa, GE Medical Systems, Milwaukee, WI). DWI was performed using a multislice, isotropic, single-shot EPI sequence, with  $B_{max}$  of 1,000 sec/mm<sup>2</sup>. Single-shot gradient echo EPI perfusion imaging (repetition time [TR]/ echo time [TE], 2,000/60 msec) was obtained with a 20 mL gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA) bolus, power injected at 5 mL/sec. Up to 17 5-mm slices were recorded with a 2-second repetition rate, giving whole brain coverage. Several pixel-by-pixel analyses, based on the concentration of the Gd-DTPA contrast agent (tracer) in each pixel with each repetition, were undertaken. Cerebral blood volume maps showed the concentration of contrast material in each pixel (corresponding to the area under the curve when calculating tracer concentration over time). Mean-transit-time maps showed relative time of arrival and departure of concentration from a given region, and time-to-peak maps showed the time to peak concentration of tracer in each pixel. We used timeto-peak maps to determining the extent of hypoperfused brain.<sup>13</sup> All measures were relative to homologous regions in the contralateral (normal) hemisphere.

Data analyses. Total lesion volumes (in  $cm^3$ ) on DWI and MRPI were determined by a technologist blinded to the results of cognitive testing. The borders of abnormality on each 0.5-cm slice of DWI or MRPI were identified on the computer monitor, outlined with the curser, then calculated using the Scion Imaging program (Scion Corp., Frederick, MD). MRPI scans were analyzed in color to highlight the contrast between hypoperfused and normal tissue. The areas of abnormality in  $cm^2$  on each slice were summed, and then multiplied by the width of each slice to determine the volume in  $cm^3$ . Pearson correlations (using Microstat-II; Ecosoft, San Diego, CA) were calculated for 1) the volume of abnormality on DWI and the total score on the cognitive battery and 2) the volume of abnormality on MRPI and the total score on the cognitive battery.

**Results.** Cognitive correlates of hypoperfused regions. A total of 40 patients (29 patients with dominant hemisphere stroke and 11 patients with nondominant stroke) were studied. For patients with dominant hemisphere stroke, the Pearson correlation between the volume of abnormality (acute infarct) on DWI and the total rate of errors on the lexical battery was significant (r = 0.55; p < 0.01). However, the Pearson correlation between the volume of abnormality on MRPI and the total rate of errors on the lexical battery was substantially higher (r = 0.65; p < 0.001; figure 1).

For patients with nondominant hemisphere stroke, there was a low (nonsignificant) Pearson correlation between the volume of acute infarct on DWI and the total rate of errors on the neglect battery (r = 0.54; p = 0.14). In contrast, the Pearson correlation between the volume of abnormality on MRPI and the total rate of errors on the neglect battery was quite high (r = 0.84; p < 0.01; figure 2). That is, the perfusion abnormality defined by MRPI predicted (and accounted for) cognitive deficits in hyperacute stroke more reliably than the acute infarct defined by DWI.



Figure 1. Total rate of errors (errors/maximum score  $\times$  100) on the lexical battery as a function of volume of abnormality on MR perfusion imaging (MRPI) in patients with dominant hemisphere stroke.

Of the 29 patients with dominant hemisphere stroke, 25 had lexical deficits (>10% errors on one or more of the tasks). In these 25 patients, DWI showed no abnormality in two (8%) aphasic patients and only a subcortical abnormality in 10 (40%) aphasic patients. In contrast, MRPI showed extensive cortical involvement in all the aphasic patients (figure 3 shows an illustrative case). In three cases, the infarcts were limited to the basal ganglia; in other cases the infarcts involved the subcortical white matter. There were no patients in this group with infarcts limited to the thalamus. Similarly, of the 11 patients with nondominant stroke, nine had hemispatial neglect; six of these nine had only subcortical infarct on DWI. Nevertheless, all nine patients with hemispatial neglect had regions of cortical hypoperfusion (see figure 3 for an illustrative case). Thus, their hemispatial neglect in the hyperacute period might be attributable to the cortical hypoperfusion, rather than the subcortical infarct itself.



Figure 2. Total rate of errors (errors/maximum score  $\times$  100) on the neglect battery as a function of volume of abnormality on MR perfusion imaging (MRPI) in patients with nondominant hemisphere stroke.



MRPI

DWI

Cognitive correlates of reperfused regions. To test the hypothesis that the radiographically defined penumbra (the diffusion-perfusion mismatch) corresponds to a region of functionally salvageable tissue, 10 patients (nine with dominant and one with nondominant hemisphere stroke) had repeat DWI, MRPI, and FLAIR 3 days after the initial testing. A subset of six of these patients were tested before and after intervention to restore blood flow to hypoperfused regions. Two patients with hypoperfusion (by MRPI) but no infarct (by DWI) in Wernicke's area were treated with pharmacologic blood pressure elevation using IV phenylephrine. Blood pressure elevation was associated with reperfusion of Wernicke's area documented by repeat MRPI during treatment, and improved auditory comprehension and naming in each patient, as reported in a separate paper.<sup>14,15</sup> In two other patients, blood pressure elevation was achieved more conservatively, with fluids and discontinuation of antihypertensive medication, and at least temporary improvement in language was achieved. In the two cases described below, reperfusion was achieved by urgent carotid endarterectomy (CEA). In the remaining four patients, there was no specific intervention to restore perfusion (and there was no spontaneous reperfusion).

For the nine patients with dominant hemisphere stroke, there was a marginally significant correlation between the volume of infarct on repeat DWI and the rate of errors on repeat language testing (r = 0.75; Student's *t*-test = 3.0; p < 0.05). In contrast, there was a striking correlation between the volume of hypoperfused tissue on repeat MRPI and the rate of errors on repeat language testing (r = 0.93; Student's *t*-test = 7.0; p < 0.003). Correlation between error rate and volumes of abnormalities on the scans could not be calculated for nondominant stroke, as only one patient with nondominant stroke had repeat testing. However, her case and a similar case of a patient with dominant hemisphere stroke illustrate the association between reperfusion and impaired function, and between reperfusion and restored function.

Patient 1. A 50-year-old, right-handed, hypertensive woman presented with sudden-onset left facial weakness and left arm clumsiness. These symptoms resolved over a few hours, but neurologic examination revealed persisting left hemispatial neglect. Conventional MRI showed subcortical white matter ischemic changes, predominantly in the Figure 3. (A) Diffusion-weighted imaging (DWI) and MR perfusion imaging (MRPI) scans of a righthanded man with hyperacute fluent aphasia due to left middle cerebral artery stenosis. His severe deficits in all language modalities were better explained by hypoperfusion of temperoparietal cortex than by the relatively small subcortical infarct on DWI. (B) DWI and MRPI scans of a 69-year-old right-handed woman, 4 to 9 hours after onset of left hemiparesis and left hemispatial neglect. Her hemispatial neglect was likely a manifestation of hypoperfusion of the right parietal cortex rather than infarction in the subcortical white matter. Note: on these grayscale renditions of colored figures, hypoperfused tissue appears darker than normally perfused tissue.

right parietal lobe, and extracranial stenosis of the right internal carotid artery (ICA). Angiography confirmed 99% stenosis of the right ICA. Over the next 9 days, before and after CEA, the patient was tested daily on matched forms of the neglect battery. In addition, she read aloud lists of 84 words matched for frequency, length, concreteness, and grammatical word class presented in standard horizontal print, vertical print (top to bottom), and mirror-reversed print, and spelled aloud to her. On initial testing, she made 3% errors in reading horizontal print, all on the left side of words (e.g., drab misread as "crab"), but no errors in reading vertical print or in recognition of words spelled aloud (table 1). In reading mirror-reversed words, she made errors on the final letters of the word (the left side of the stimulus, but the right side of the internal representation of the word). In a gap-detecting task on the left or right half of a circle, she was more accurate in detecting right-sided than left-sided (100% versus 70%) gaps in circles presented in isolation (such that the gap was on the far right or left of the stimulus). Over the next few days, while she awaited CEA, her hemispatial neglect worsened. For example, her drawing of a clock deteriorated from subtle spacing errors to omission of all of the numbers on the left.

Diminishing perfusion of the right parietal lobe was the suspected cause of her worsening neglect. MRPI and DWI confirmed that she still had a substantial diffusionperfusion mismatch. She therefore underwent urgent right CEA. Less than 12 hours after CEA, repeat testing on the neglect battery and all of the previous reading lists showed

Та	ıble	1	Patient	1's	"neglec	t dysl	lexic'	' errors	in	readin	lg
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Standard prir	nt	Mirror-reversed print		
Stimulus	Response	Stimulus	Response	
rice	"price"	chef	"chess"	
forget	"get"	bust	"bus"	
recall	"well"	rain	"raid"	
rain	"brain"	feet	"feel"	
feet	"beet"	sink	"sing"	
sink	"rink"	blender	"blend"	



Figure 4. Patient 1's rate of "neglect dyslexic" errors (errors/maximum score  $\times$  100) on alternate forms of the word reading test before and after carotid artery endarterectomy (CEA).

complete resolution of hemispatial neglect (normal clock drawing; <1% reading errors; no errors in gap detection). Her prior deterioration on these tasks was completely reversed after CEA (figure 4).

The day before CEA, MRPI showed an area of hypoperfusion (delayed bolus arrival times, revealed by time-topeak maps) in the right parietal lobe substantially larger than the infarct visualized on DWI and T2-weighted images the same day (figure 5). The infarct was confined to area 39 (the angular gyrus), but the perfusion abnormality extended anteriorly to involve area 40 (the supramarginal gyrus) as well as area 39. Repeat MRPI the day after CEA showed marked reduction of the perfusion abnormality, now involving only area 39 (see figure 5). These scans confirmed resolution of the hypoperfusion in area 40 (the supramarginal gyrus), coincident with resolution of her hemispatial neglect coincident with the resolution of ischemia.

Patient 2. A 59-year-old right-handed man presented with a severe impairment in accessing the meanings of words (a "lexical semantic" impairment), indicated by the production of semantically related word errors in all lexical tasks. For example, he named a book a "leaflet" and a pencil a "pen." He accepted the word "fork" as the name for a pictured knife and the word "turtle" as the name of a pictured snake. Similarly, he accepted the written word *coat* as the name for a pictured shirt and the word *rabbit* as the name of a pictured mouse. This deficit progressed rapidly over the course of 3 days. A carotid ultrasound at an outside hospital indicated severe left ICA stenosis. He



Figure 6. Diffusion-weighted imaging (DWI) and MR perfusion imaging (MRPI) scans before and after carotid artery endarterectomy (CEA) in Patient 2.

was transferred to our hospital on day 3, where angiogram confirmed 95% stenosis of the left ICA and 75% stenosis of the right ICA. DWI showed only tiny infarcts in the frontoparietal white matter, in the watershed distribution between the left anterior and left middle cerebral arteries. In contrast, MRPI showed that the entire distribution of the left ICA was severely hypoperfused (figure 6). His large region of hypoperfusion, involving the entire left frontotemperoparietal region, could better account for his global aphasia than his tiny white matter infarcts. In view of the substantial diffusion-perfusion mismatch, indicating a large area of salvageable tissue (believed to be responsible for his global aphasia and right hemiparesis), he underwent urgent CEA. Immediately after surgery, his aphasia and hemiparesis resolved (table 2). Postoperative MRPI showed complete reperfusion of the left ICA territory (see figure 6).

**Discussion.** The data from this investigation allow two primary conclusions with important clinical implications. First, this study demonstrated that in many cases of "cortical" deficits (aphasia or hemispatial neglect), the hyperacute infarct was limited to



Figure 5. (A) Diffusion-weighted imaging (DWI) and MR perfusion imaging (MRPI) scans in Patient 1, when she showed worsening left hemispatial neglect. (B) MRPI after carotid artery endarterectomy (CEA).

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Task	Before CEA	After CEA	
Picture naming	0%	100%	
Tactile naming	47%	100%	
Auditory word–picture matching	53%	100%	
Written word–picture matching	47%	100%	
Written naming	0%	84%	

CEA = carotid endarterectomy.

the subcortical tissues, and there was concurrent cortical hypoperfusion in each case. Similar results have been reported using SPECT (regional cerebral blood flow, regional cerebral blood volume) or fluorodeoxyglucose PET 3 or more days after onset of aphasia or neglect in patients with structural lesions restricted to subcortical areas.<sup>5,16-19</sup> Thus, cortical hypoperfusion probably accounts for at least some of the reported cases of aphasia or hemispatial neglect due to acute or subcortical stroke.<sup>20,21</sup> For example. we reported data from an acute stroke trial showing that 69% of patients with acute aphasia (without neglect) and 74% of patients with acute hemispatial neglect (without aphasia) had infarcts on follow-up CT that were limited to subcortical regions.<sup>22</sup> Although some of these cases may have been due to the subcortical infarct itself,23-25 many such cases of acute aphasia or neglect are likely due to hypoperfusion of cortical regions in the early stages of stroke. Unlike previous studies, here we were able to demonstrate that acute intervention that successfully reperfused the cortex was associated with simultaneous recovery of the language or cognitive deficit (within 12 hours of intervention, when both MRPI and cognitive testing were repeated), providing stronger evidence that the hypoperfused cortical regions were responsible for impairment. In at least one case, there was also reperfusion of subcortical tissue that might have also contributed to the observed improvement.

Second, DWI and MRPI together provide an estimate of the extent and site of potentially recoverable tissue that corresponds to reversible clinical deficits in acute stroke. Quantitative analyses of the data showed that the rate of errors on the cognitive battery was more strongly correlated with the volume of abnormality on MRPI than the volume of abnormality on DWI. This result is consistent with previous studies showing that MRPI corresponds more reliably than DWI to the clinical presentation (using the Canadian Neurologic Scale7,13 or the NIH Stroke Scale<sup>7,26</sup>) and provides additional empirical evidence for the hypothesis that MRPI reveals regions of the brain that are not only oligemic but also dysfunctional. Furthermore, the two case presentations demonstrate that the diffusion-perfusion mismatch delineated regions of functionally reversible ischemia due to poor perfusion. In each case, hypoperfusion was reversed by CEA, and function was restored in <12 hours. Although the recovery could have been due to reorganization, the fact that both patients were functionally deteriorating prior to intervention and recovered abruptly after intervention suggests that the resolution of deficits was due to reperfusion (seen on MRPI). Similar results were obtained when reperfusion was achieved by blood pressure manipulation 3 to 7 days after onset of initial symptoms, in patients with large-vessel intracranial disease.<sup>14</sup> Although many authors have proposed that the diffusion-perfusion mismatch represents the ischemic penumbra of potentially recoverable tissue,<sup>6,26-28</sup> the validity of this concept for the management of acute stroke depended on demonstrating that the radiologically defined penumbra corresponds to tissue that is both dysfunctional and salvageable, as we have done here. Although the combination of CT with either SPECT, PET, or CT perfusion can provide the comparable information, DWI plus MRPI (coregistered with T2-weighted images done at the same time) provides better spatial resolution, and DWI is more sensitive than CT to nonviable tissue in the hyperacute period. And although we demonstrated an ischemic penumbra of salvageable tissue as late as 7 days after onset of symptoms, the penumbra is generally thought to last for only a few hours. Thus, scans such as DWI and MRPI together, which can distinguish viable from nonviable tissue in the first few hours, are crucial for identifying the best candidates for reperfusion therapy.<sup>7,26,28</sup> It is also seems, from the two cases reported here, that a substantial mismatch between DWI and MRPI that persists for a few days after stroke (and is associated with functional deficits) in patients with severe carotid stenosis might identify those who might show functional gains with urgent CEA. That is, in patients with a diffusion-perfusion mismatch it might be advisable not to wait the traditional 6 weeks or so after stroke to perform CEA. However, this hypothesis needs to be confirmed with larger, and randomized, controlled studies.

Finally, the reported cases of reperfusion also illustrate how MRPI might be useful in revealing the neuroanatomic regions crucial to specific cognitive functions. For instance, Patient 1's case yields evidence that the supramarginal gyrus is essential for some types of spatial attention: she had hemispatial neglect when the right supramarginal gyrus was hypoperfused, and this neglect resolved when the supramarginal gyrus was reperfused after CEA. MRPI plus DWI before and after reperfusion thus allows identification of the sites of temporary dysfunction responsible for specific cognitive impairments in previously normal subjects, before to the opportunity for reorganization.

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