

DIFFUSION-WEIGHTED IMAGING: CAN IT PLAY A ROLE IN THE EVALUATION OF PATIENTS WITH EPILEPSY?

Diffusion-Weighted and Perfusion MRI Demonstrates Parenchymal Changes in Complex Partial Status Epilepticus

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Diffusion-weighted MRI (DWI) and perfusion MRI (PI) have been mainly applied in acute stroke, but may provide information in the peri-ictal phase in epilepsy patients. Both transient reductions of brain water diffusion, namely a low apparent diffusion coefficient (ADC), and signs of hyperperfusion have been reported in experimental and human epilepsy case studies. We studied 10 patients with complex partial status epilepticus (CPSE) with serial MRI, including DWI and PI. All patients showed regional hyperintensity on DWI, and a reduction of the ADC in (i) the hippocampal formation and the pulvinar region of the thalamus (six out of 10 patients), (ii) the pulvinar and cortical regions (two out of 10), (iii) the hippocampal formation only (one out of 10), and (iv) the hippocampal formation, the

pulvinar and the cortex (one out of 10). In all patients, a close spatial correlation of focal hyperperfusion with areas of ADC/DWI change was present. In two patients, hyperperfusion was confirmed in additional SPECT (single photon emission computed tomography) studies. All patients received follow-up MRI examinations showing partial or complete resolution of diffusion and perfusion abnormalities depending on the length of the follow-up interval. The clinical course, EEG, and SPECT results all indicate that MRI detected changes related to prolonged epileptic activity. Combined PI and DWI can visualize haemodynamic and tissue changes after CPSE in the hippocampus, thalamus, and affected cortical regions.

COMMENTARY

Prolonged seizures and status epilepticus (SE) can cause cytotoxic and vasogenic edema in the epileptogenic area (1). Diffusion-weighted magnetic resonance imaging (DWI) is a novel technique that, at a microscopic level, can identify differences in the variation of molecular water mobility in extracellular spaces, thus delineating focal areas of cytotoxic edema of various causes. These differences are expressed quantitatively as changes in the apparent diffusion coefficient (ADC) and qualitatively as changes in DWI signal intensity at the presumed epileptogenic area identified by visual examination (2,3). An intracellular water flux in the epileptogenic area will cause contraction of the extracellular spaces during prolonged epileptic activity, resulting in a decrease of the ADC and an increase in signal intensity in the DWI. The opposite changes would take place in areas of neuronal cell loss, such as occurs with mesial temporal sclerosis (2,3).

It is not surprising that various groups of investigators have examined the utility of using DWI to localize the epileptogenic zone for patients with partial epilepsy in the course of SE or during its postictal period. The study by Szabo et al. demonstrates the value of peri-ictal DWI in identifying not only the epilep-

togenic zone in complex partial SE but also the subcortical areas of propagation, such as the pulvinar thalamic nuclei. Kim et al. reached similar conclusions in a study of four patients who underwent a DWI within 3 days of the onset of SE (three patients had complex partial and one patient had generalized SE) (4). These investigators did not find changes in thalamic nuclei, however. In both studies, DWI and MRI were repeated several weeks after remission of SE revealed complete resolution of the area of increased signal intensity, which was replaced by focal atrophy in some patients. Whether abnormal findings on DWI are predictive of focal atrophy is yet to be established.

The study by Kim et al. also included three patients who had experienced a generalized tonic-clonic seizure lasting between 8 and 10 minutes and who had undergone a DWI 2–3 days after their seizure. In contrast to patients who experienced SE, mild changes in ADC and signal intensity were identified in only one patient. Likewise, in a study of eight patients with pharmacoresistant temporal lobe epilepsy (TLE), Diehl et al. performed a DWI between 45 and 150 minutes following single, short seizures documented on video-EEG recordings (5). Among the eight patients, six had mesial temporal sclerosis, one had a brain tumor of unknown type, and one had a normal MRI. DWI yielded significant decreases in the ADC in only one of the six patients with mesial temporal sclerosis as well as in the patient with a brain tumor.

Do these data suggest that DWI is only useful in detecting the epileptogenic area in SE? After all, DWI does not appear to add anything to the localization yield of other functional neuroimaging studies, such as ictal single photon emission tomography (SPECT). For example, Tatum et al. carried out a ^{99m}Tc -HMPAO SPECT on six patients with SE (documented by EEG recordings) and six patients with other neurologic diagnosis (6). All six patients with SE at the time of the SPECT demonstrated an area of focal hyperperfusion that corresponded to the epileptogenic area established with EEG recordings. In contrast, none of the patients with other neurologic disorders had an area of increased perfusion. Clearly, neurologists must be aware of the SE-related changes in signal intensity in DWI studies to avert false negative diagnosis of complex partial SE and unnecessary invasive studies to clarify the nature of such areas of increased signal. Clinicians must also remember that partial SE can yield similar findings with T_2 -weighted images and fluid recovery attenuation recovery (FLAIR) sequences on standard MRI studies (4).

The other important question is whether interictal DWI has any role in the evaluation of patients with partial epilepsy. In other words, how often do DWI studies reveal an increase in ADC in the epileptogenic area? The data available to date suggest mixed results with respect to the localizing yield of interictal DWI in TLE. Lee et al. carried out interictal DWI studies in 20 patients with mesial TLE and 19 normal volunteers (7). Visual examination failed to lateralize the epileptogenic area in any of the patients. Calculation of the ADC showed significant increases (relative to the ADC of normal volunteers) in the mesial temporal area ipsilateral to the seizure focus in all patients; these changes, however, failed to differ significantly from those on the contralateral side in all patients. In contrast, two other interictal studies using DWI-yielded results more favorable to localizing the epileptogenic area. Hugg et al. generated ADC maps in eight patients with intractable mesial TLE (8). In all eight patients, they found that ADC was significantly elevated in the ictogenic hippocampus (determined electrographically and with corroboration from volumetric MRI studies). Yoo et al. carried out interictal DWI studies in 18 patients with mesial temporal sclerosis and 19 normal controls (9); they found that the mean ADC value measured at the hippocampal area was significantly higher on the ictogenic side than on the contralateral side. The overall correct lateralization rate of ADC was 100%. In the patients, the mean ADC in sclerotic hippocampi was significantly higher, and the normal-appearing hippocampus of the contralateral side had significantly higher ADC values compared with those of healthy volunteers. In contrast, visual assessment of DWI images failed to lateralize the lesion in all patients.

In partial epilepsy, the ultimate "gold standard" for DWI to identify and localize the epileptogenic area is complete seizure remission after resection. Here again, the data show mixed re-

sults. For example, Kantarci et al. carried out interictal DWI and proton magnetic resonance spectroscopy (^1H MRS) studies in 40 patients with intractable TLE, who went on to have a temporal lobectomy, and in 20 normal subjects (10). DWI appeared to be able to localize the epileptogenic area more frequently than ^1H MRS (increased ADC at the hippocampus in 80% of patients; increased ADC at the temporal stem in 65% versus abnormal ^1H MRS in 45% of patients). Yet, all but one patient (94%) in whom ^1H MRS lateralized to the side of surgery were seizure-free, while lateralization of the side of surgery with DWI was not associated with a better seizure outcome.

Of note, the magnitude of DWI changes has also been correlated with other diagnostic tests (e.g., neuropsychological tests) used to evaluate the functional status of temporal lobe structures. Indeed, Liu et al. performed interictal DWI and a neuropsychological evaluation on 20 patients with intractable TLE as well as on 20 age- and sex-matched controls (11). Significantly higher ADC was identified in all patients relative to controls over the whole brain, and in particular in the hippocampi and the parahippocampal gyri. In addition, patients had significantly higher ADC within the ictogenic hippocampus and parahippocampal gyrus than in the contralateral side. Finally, significantly negative correlations were seen between hippocampal ADC and scores of various memory tests.

Finally, there is some suggestion that the localizing yield of interictal DWI may be enhanced with hyperventilation. At baseline and after two 4-minute periods of hyperventilation, Leonhardt et al. carried out interictal DWI on ten patients with TLE (four of whom had mesial temporal sclerosis and six had idiopathic TLE) and compared them with 10 normal controls (12). Compared to controls, the 10 patients had higher baseline ADC in the ictogenic hippocampus. Hyperventilation resulted in further significant increases of ADC in patients with mesial temporal sclerosis but not in the six patients with idiopathic TLE.

In conclusion, these data clearly suggest that peri-ictal DWI can yield localizing data of the epileptogenic zone in SE of focal origin. The role of interictal DWI in the presurgical evaluation of refractory partial epilepsy, particularly TLE, seems promising. However, further studies are needed to establish the limitations of its localizing yield, above all for idiopathic TLE, for which other neuroimaging studies fail to contribute any localizing data.

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