The *American Journal of Neuroradiology*: Expanding Its Vision, Extending Its Reach

Behind the scenes, and perhaps unnoticed by readers, many changes have occurred in the *AJNR* regarding editorial structure, scientific content, and dissemination of published material. Changes in a journal should proceed thoughtfully and deliberately, and should be guided by what a journal such as ours wants to accomplish. The intent of this end-of-the-year editorial is to give our members and subscribers a flavor of what has recently been implemented and what we may expect in the future.

Readers of this issue of the *AJNR* will note that there has been a change in the masthead of the journal. Not only have we added 28 new members to the Editorial Board, but the disciplines represented have increased, and the geographical distribution of the members has widened. The pivotal role neuroimaging plays in the clinical neurosciences, the ever-expanding use of neurointerventional procedures in neurovascular disorders, and the burgeoning use of a variety of image-guided, provocative spinal examinations and therapeutic procedures makes it imperative that there be a significant input from the fields of neurology, neurologic surgery, and orthopedic surgery in our journal. This has been accomplished by having these disciplines represented on our Editorial Board, and a glance at the masthead will show the inclusion of such physicians from these medical disciplines. These new Editorial Board members will be frequent reviewers of submitted manuscripts, occasional editorialists, and they will help us keep our feet rooted in our primary goal, which is to disseminate new and important information in the science of neuroimaging, the end result of which is improved patient care.

Advances in neuroradiology depend to a large measure on the creativity of our colleagues in the basic sciences. For the design of neuroimaging equipment, implementation of innovative software programs, the conceptualization and development of new material used in interventional procedures, and advances in image transfer and display, we rely on physicists, biochemists, and engineers, among others, and these disciplines are now also represented by our Editorial Board. Authors who focus primarily on these topics can expect to have their work evaluated by scientists in their field whom we have added to our list of peer reviewers. In essence, the *AJNR* will continue not only to maintain its leadership role in clinical neuroimaging, but it will strive to add significantly to the publication of basic research in medical imaging. Those in the basic sciences must understand what neuroradiologists wish to achieve, and likewise, those involved in neuroimaging must be familiar with the ever-changing landscape in basic research. The *AJNR* is the perfect vehicle for the interchange of ideas between clinicians and scientists involved in neuroimaging.

An unmistakable increase in international representation of papers submitted and eventually published in the *AJNR* has occurred over the past few years. During the first 6 months of 2000, for example, over half of the submitted papers came from outside North America. The reasons for the increasing submission primarily from Europe and Asia are multifactorial, and this situation will in part be discussed at one of the focus sessions of the 2001 ASNR annual meeting in Boston this spring. Although the number of subscribers outside of North America does not match the high rate of non-American publications in the journal, the worldwide interest in the *AJNR* continues to rise and the message is that, although the name of the journal is the *''American'' Journal of Neuroradiology*, it is in all senses an international journal. Because of this important and growing influence on the *AJNR* of contributors from around the globe, there now are 11 members of the Editorial Board from outside North America. They not only will bring their expertise to bear on the journal, but they may give our readers a perspective on advances in neuroradiology from many different regions of the world, and how patient care is thereby altered.

As of September 2000, the *AJNR* has begun on-line publication (www.ajnr.org). There are numerous advantages of an on-line journal, such as linkages to other journals, quick retrieval of previously published papers, rapid dissemination of journal issues, and the ability to reach subscribers, particularly those abroad, whose mail delivery systems are not optimal. Despite all these advantages, the printed version of the journal will remain intact for the foreseeable future, as it is often more convenient because of its portability, is easier on the eyes, can be read more quickly, and long-term archival matters are more easily handled. Importantly, authors just like to see their article in print.

Simultaneously with the move to electronic publication, changes will occur in the way the journal is managed, the way authors submit papers, and the way manuscripts are evaluated. Dealing with mountains of paper from time of submission through the review process to the revision stage and to final production is inefficient and results in a slow turnaround of manuscripts. The *AJNR* has begun experimenting with electronic peer review, and although more mature and friendly systems are still needed, it is possible that many of our reviewers

will be evaluating manuscripts on-line, and authors will receive decisions more quickly.

As we all know, the electronic dissemination of information is occurring at such a rapid rate that predicting where we will be in the intermediate to long-term future is fraught with uncertainty. Although a rapid distribution of articles has its greatest impact in disciplines such as physics or biological chemistry, where late-breaking discoveries can influence the research of others, there is also the need in neuroimaging and neurointervention to have important observations and techniques in the hands of our members as rapidly as possible. Subscribers could be notified by e-mail when articles in which they have particular interest have been electronically posted. To extend this concept even further, it would be possible to combine articles from different journals that explore the same topic and ''deliver'' these papers to designated subscribers. One can envision, for example, an interventional neuroradiologist receiving specified articles from multiple journals—the *AJNR, Neurosurgery*, the *Journal of Neurosurgery, Stroke*—as they come on-line. Similarly, a neuroradiologist with a particular interest in spine imaging and therapeutics would preferentially receive papers from the *AJNR, Spine*, and the *Journal of Bone and Joint Surgery*. Targeting specific audiences with multiple journal input is on the horizon.

Of course the economics and the administrative details from the standpoint of a journal, a society, and a publisher must be clearly worked out; these may be the most difficult obstacles to overcome. The more easily and widely distributed articles become, the more beneficial this is to a given specialty; however, the publishers of such material, who see these papers primarily as a commodity and see erosion of their control of the end product, may begin to raise legitimate economic concerns.

From strictly an educational and teaching standpoint, electronic publishing has major advantages. Video clips can be imbedded into articles that, for example, may illustrate endovascular techniques or percutaneous spine procedures. On-line discussions with authors would allow an open dialogue, which could be shared with the journal's subscribers.

It is difficult at the end of the year 2000 to know what the journal will look like 5 years from now, but it is certain that the science will be distributed more quickly over a greater geographical area, and it will be displayed in a more interesting and usable format. We are now taking the first steps to achieve those goals.

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Further Explanations for the Formation of Syringomyelia: Back to the Drawing Table

The etiology of nontraumatic spinal cord cysts remains unclear. Many explanations have been offered, though most have never been validated. Most of the proposed hypotheses, however, have something in common. They all invoke the possibility of abnormalities in the subarachnoid space that surrounds the spinal cord where a syrinx is present. Lesions such as extramedullary tumors, arachnoiditis, and vascular compromise have been found in conjunction with spinal cord cysts. In this issue of the *AJNR* (page 1785), the article by Brugières et al entitled *CSF Flow Measurement in Syringomyelia* provides some new insights regarding the abnormal flow of CSF, both inside and outside a syrinx.

The authors of another recent article proposed that the status of the spinal cord's central canal was ultimately responsible for the features of syrinxes (1). That is, a patent canal may lead to an extensive syrinx, a canal that is only segmentally patent may lead to a focal syrinx, and a nonpatent canal may lead to cord edema. Regardless of the end result (extensive or focal cysts), if the patients are symptomatic, then treatment is needed.

Brugières et al showed that greater alterations in intracystic fluid velocity are seen in large cysts. They found that the pericystic CSF velocity was not significantly different in small (and mostly asymptomatic) cysts than in large (and mostly symptomatic) cysts. This last observation is at odds with the currently favored explanation of abnormal CSF flow in the subarachnoid space as the factor leading to syrinx formation. In addition, Brugieres et al found a significant lack of association between CSF velocities (both inside and outside of the cysts) and factors such as cyst size and symptoms. The only factors that correlated were a higher diastolic cyst velocity with more severe symptoms. I have always entertained the idea that intracystic fluid motion is mostly turbulent and disorganized, and that this may result in expansion of some cysts. Brugières et al found that the intracystic fluid clearly has systolic and diastolic velocity peaks. This suggests a type of ''organized and sequential'' motion of the intracystic fluid. Although this pattern of motion mimics that of the CSF in the pericystic subarachnoid space, it may not be induced by it. This is reflected by the findings of Brugiéres et al, who identified an earlier peak systole inside the cyst rather than outside of it, which implies that intracystic fluid motion may be independent from fluid motion in the subarachnoid space. In addition, there were no differences in subarachnoid space

fluid motion between patients with a syrinx and healthy control subjects.

We can probably assume that fluid pulsatility originates in the cord secondary to its blood flow (the same phenomenon drives CSF out of the lateral ventricles in the brain). Because a syrinx has already expanded the cord and narrowed the subarachnoid spaces, the pulsations will be transmitted first and preferentially to the cyst. Since water is noncompressible, the cyst then transmits its pulsations to the subarachnoid space. This may not happen under normal circumstances in which most of the spinal cord pulsations are absorbed by the fluid in the subarachnoid space. Based on these data, it seems possible that some spinal cord cysts are a primary spinal cord disorder, not originating as a consequence of an abnormal subarachnoid space.

How does fluid accumulate initially inside the cord? Fischbein et al (1) thought that the initial entrance of fluid into the cord reflected an abnormality of the subarachnoid space, driving CSF into the cord through the perivascular spaces. In view of the data shown by Brugières et al, I would like to reconsider that explanation. Some believe that the Virchow Robin spaces may contain a small amount of CSF, and that it is possible the CSF enters these spaces from the subarachnoid space. Subsequently, expansion of the cord (as a result of the normal, alternating arterial and venous blood filling) normally ''milks'' this fluid from the cord into the subarachnoid space. An abnormal subarachnoid space prevents this type of flow, leading to accumulation of CSF within the cord. This fact is, however, at odds with current evidence that the perivascular spaces of the CNS are sealed from the subarachnoid space (for example, they do not contain blood in cases of subarachnoid hemorrhage, regardless of their size) (2). If this is true, invoking abnormalities of the subarachnoid space as the etiology for syringomyelia in some cases is probably wrong. Again, these data can only lead to a proposal that at least some syrinxes are caused by intrinsic cord abnormalities, which at this time are not clear. The fact that diastolic velocities are higher in symptomatic large cysts is also important. Peak systole is transient, but the pressure exerted during diastole is omnipresent. Thus, it is not surprising that larger and more symptomatic cysts have a higher diastolic velocity.

Consider what happened to Brugières et al's patients after surgery. After decompression of remote lesions, such as a Chiari type 1 malformation, the intracystic fluid velocities (including diastolic velocity) decreased. After syrinx decompression, the systolic peak was first observed in the subarachnoid space and then within the cord (a reversal to normal). Again, it seems as if the status of the spinal cord determined the neighboring fluid dynamics and not vice versa.

I am not discounting the possibility that some syrinxes are due to an abnormal subarachnoid space. I have seen syrinxes associated with concurrent or remote spinal canal masses, following meningitis, and as sequelae of surgery. In many of these situations, an abnormal subarachnoid space was probably the fundamental etiology. As for many other disease processes, the etiology of syringomyelia is probably multifactorial. The importance of the article by Brugières et al lies not in showing abnormal fluid flow in the cysts and surrounding spaces, or in showing a reversal of these abnormalities after therapy. The importance of this article is that it forces us back to the ''drawing table'' to try to come up with other explanations for the formation of the syringomyelia.

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Is There Room for MR Imaging in the Assessment of Hereditary Motor and Sensory Neuropathies?

Hereditary motor and sensory neuropathies (HMSN) are a group of neurologic diseases, which are highly heterogeneous in terms of both their genetic background and their pathologic and clinical manifestations. In the past 3 decades, considerable advances in the understanding of this group of disorders have been made, which formed the basis for their classification and diagnosis. At present, diagnosis of HMSN is based on information derived from its mode of inheritance and clinical course, as well as from neuropathological, neurophysiological, and molecular genetic findings.

In the past few years, based on the concept that MR imaging is a noninvasive way to look at nervous system pathology, a question has been raised as to whether there is any room for MR imaging in the assessment of HMSN. Several preliminary case reports showed that MR imaging has the potential to detect enlarged nerve roots in those types of HMSN that are known to determine hypertrophic nerve changes. Nerve root enlargement on MR images is, however, a disease-nonspecific sign, and, as a consequence, the detection of nerve root enlargement on MR images does not modify the

''classical'' approach to diagnosis and classification of HMSN. It is not surprising, therefore, that when reading through the MR literature on HMSN the primary conclusion is that the role of MR imaging in the assessment of these disorders can only be marginal, and that these studies are driven more by the increased availability of MR scanners rather than by a clinical need or a genuine research interest.

One of the major merits of the article by Cellerini et al published in this issue of the *AJNR* (page 1793) is to mitigate this negative feeling. This study provides a systematic MR evaluation of the cauda equina and intradural nerve root abnormalities from a series of 10 patients with type I, II, and III HMSN. It also presents correlations between MR imaging and histopathological findings from sural nerve biopsy. The study confirms that MR imaging has the potential to detect enlarged nerve roots in patients with type I HMSN, in the absence of palpable peripheral nerve enlargement. This change was found to be associated with the presence of onion bulbs in the sural nerves. Most important, however, is that nerve root enlargement was observed in two patients with atypical clinical manifestations (consisting of progressive urinary bladder dysfunction and severe low back pain), suggesting a clinically meaningful role for MR imaging in the diagnosis of, at least, some cases of type I HMSN. Although interesting, the value of this observation in clinical practice is questionable. Diagnostic MR imaging is, in fact, usually obtained in the context of undiagnosed clinical conditions, and one might argue whether subtle changes of nerve root size, potentially useful to suggest a diagnosis of type I HMSN, would be detected in patients with no clinical suspicion of having such a disorder.

This study also shows that diffuse enhancement of intradural nerve roots is a relatively frequent finding in patients with type I and III HMSN. Because no inflammatory changes of the sural nerves from these patients were seen histopathologically, nerve root enhancement in these conditions is likely to be secondary to blood-nerve barrier increased permeability, which in turn may be the result of either blood-nerve barrier congenital defects or ongoing demyelination. Interestingly, enhancement was not seen in the two patients with type II HMSN. If confirmed by larger patient series, this is another potentially relevant finding of the study by Cellerini et al. Although genetic, neuropathological, and neurophysiological findings are different in patients with type I and type II HMSN, they are, in fact, virtually undistinguishable in terms of clinical findings and course. Therefore, it is tempting to speculate that nerve root enhancement in the context of HMSN might be helpful in distinguishing patients with type I HMSN from those with type II HMSN. Given the relatively benign course of the two conditions and the absence of any treatment option, one might, however, argue that this differentiation is no more than an academic exercise.

In clinical neurology, MR imaging is not simply a powerful diagnostic tool, but it is also an intriguing way to understand in vivo the mechanisms of a disease's manifestations and evolutions. To establish this role, however, there is a large amount of work to be done in order to link firmly MR imaging findings with histopathologic changes. Therefore, apart from the above-mentioned specific merits, the paper by Cellerini et al has another more general merit, which goes beyond the actual results of the study. The authors have shown that, although challenging (especially in CNS disorders), correlating MR imaging and histopathologic analysis might be a rewarding exercise in increasing our understanding of the pathophysiological processes of many neurologic conditions.

The study by Cellerini et al, albeit larger than previous studies on the topic, is still based on a relatively small numbers of patients. Nevertheless, the MR imaging findings reported have the potential to be clinically useful in directing physicians toward a diagnosis of type I HMSN in some atypical cases. This calls for a multicenter effort in order to collect data from larger patient samples, with the ultimate goal being able to establish the role of MR imaging in the study of HMSN rigorously. This effort would reduce the number of unnecessary MR imaging examinations as well as facilitate the diagnostic workup in some cases, such as those described by Cellerini et al. At present, the balance between these two conflicting aspects cannot be defined exactly; however, it is likely that the role of MR imaging in the assessment of patients with HMSN will remain modest.

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Diffusing into the Future

Of all of the recent functional MR techniques, there is no question that diffusion-weighted imaging has proved to be the most important. Whereas early methods were marred by technological difficulties, the advent of echo-planar imaging and improved gradients led diffusion into the spotlight. Of course, its use in the evaluation of acute infarct captured most of the early attention and still remains the most important clinical application of diffusion imaging. Other applications, however, proved the utility and robustness of the technique. These included differentiation of acute from chron-

ic ischemia in patients with diffuse white matter changes, differentiation of cystic tumor from abscess, and differentiation of epidermoid from arachnoid cyst.

At the same time, clinical diffusion imaging has proved to be somewhat unwieldy for a number of reasons. First, due to artifacts such as T2 shine through, evaluation of lesions with diffusion often required postprocessing to create apparent diffusion coefficient (ADC) maps to eliminate the T2 component. Second, even with ADC maps, large categories of lesions (such as tumor, demyelinating disease, and infection) were found to display heterogeneous behavior with diffusion imaging. For example, some infections would show little diffusion change, whereas others would display markedly restricted diffusion. In demyelinating and dysmyelinating disease, different diffusion behavior could be documented in a single lesion. Clearly, an overall schema for interpreting diffusion images, such as is available for acute infarction, remains to be developed for other entities.

Three articles in this issue of the *AJNR* suggest possible future paths for diffusion imaging. DeLano et al (page 1830) used diffusion-weighted imaging with higher b values, ranging from zero to 3500 s/mm^2, to establish normative references for signal intensity characteristics and ADCs of the adult brain. They found that increasing b values resulted in a progressive decrease in the ratio of gray matter to white matter signal intensity. Meyer et al (page 1821) studied patients with suspected brain infarction with b values from 1000 to 3000 s/mm^2. They found that increased b values did not affect the diagnosis of acute infarction substantially, but did result in a marked improvement in the detection of lesions with facilitated diffusion. Clearly, findings such as these are essential to bear in mind as we progress to the use of higher b values. Finally, Melhem et al (page 1813) examined quantitative ADCs and diffusion anisotropy brain maps using six different b values, from 0 to 800 s/mm^2, and found that the number and strength of the b values do influence measures of diffusion and anisotropy.

Some of these articles suggest a more sophisticated use of diffusion in the future. DeLano et al's finding of variability in the gray matter to white matter signal intensity ratios has deeper implications. Unlike for field strength, where image contrast remains the same for most commonly used magnets, increasing b values have a different effect, adding another layer of complexity to our study of diffusion-weighted imaging. On the other hand, both of the articles that explore the use of higher b values also promise to simplify clinical diffusion imaging. They intimate that using increased b values may free up routine diffusion-weighted imaging from its most pressing problem, T2 shine through. At high b values, as was theoretically suggested years ago, the contribution of T2 weighting decreases. Therefore, the complicated postprocessing now necessary to achieve routine ADC maps may become a thing of the past, eliminating consideration of T2 shine through.

All three articles also serve to focus more attention on the actual physiological basis of restricted and facilitated diffusion. Whereas it is easy to consider diffusion as a measure of intracellular water, and to suggest that acute infarcts appear hyperintense due to increased intracellular water, we have always suspected that approach was too simplistic. In pure water, diffusion-weighted image intensity falls exponentially as a function of the b value. In brain tissue, water occupies many different environments, so the situation is more complex. At low b values, image intensity behaves like a rapidly decaying exponential, whereas at higher b values the intensity decreases at a lower decay rate. This behavior is often termed ''biexponential'' decay. The difficulty is that there is no single diffusion coefficient that describes the system; there are two. Relatively fast diffusion accounts for the rapid decay at low b values, and slower diffusion produces the gradual decay measured at high b values. Whereas it is clear that the fast and slow components depend on the properties of brain tissue, detailed studies in animals and humans have not found a simple interpretation of the two diffusion coefficients. Although it is tempting to assign the fast component to extracellular water and the slow component to intracellular water, current models of diffusion reject this interpretation (1, 2). It is likely that several factors are important, including partial volume averaging of blood and CSF, restrictions to diffusion at several length scales, and exchange of water between compartments with different diffusion and relaxation properties.

These articles also underscore the importance of standardizing the b values used in clinical studies. The benefits of improved diffusion contrast at high b values come with the complication of prescription-dependent measures of apparent diffusion. The ADC is conventionally derived from images taken at two different b values. Because tissues are described by fast and slow components, the results of a two-point measurement will depend on the specific b values chosen. If the lower b value is set to 0 (a T2-weighted image) and the upper value is allowed to vary, then the ADC will vary as a function of the upper value. Specifically, one would expect the measured ADC to decrease as the upper b value increases. This is supported by the work of Melhem et al and DeLano et al. Both articles show that the ADC varies depending on what b values are used, and that higher b values lead to lower estimates of the ADC. Melhem et al also found that higher b values (up to 800 s/mm^2) reduce the standard deviations of the (isotropic) ADC and fractional anisotropy. This agrees with the results of Bito et al and Jones et al, who showed (in phantom and single subject experiments) that the standard deviations of diffusion estimates are minimized when the upper b value is approximately 1/ADC (3, 4).

Over all of this is superimposed the ultimate goal of imaging: the investigation of pathophysiology. Different b values may be better for the evaluation

of different diseases. For example, demyelinating lesions may have improved conspicuity at lower b values, whereas cortical lesions may be depicted better at higher b values. Although the article by Meyer et al focuses primarily on acute infarction, it also notes that the hypointense appearance of lesions with facilitated diffusion is accentuated with increasing b values. Most striking is an example of an oligoastrocytoma, which appears isointense at b = 1000 s/mm^2, but markedly hypointense at b = 2000 s/mm^2 and b = 3000 s/mm^2. Clearly, much of the advantage of increased b values may lie not with the diagnosis of lesions with restricted diffusion, especially acute infarcts, but with allowing a more complete understanding of other types of disease. For example, in demyelinating and dysmyelinating diseases, the true nature of enhancing lesions may become more obvious. The differences in the diffusion characteristics of the advancing, enhancing rim versus the central portion of the lesion may be accentuated, confirming even more strongly the behavior of these types of diseases as involving not only the destruction of myelin, but also of axons in the central core of the lesion.

Ultimately, all three articles in this issue point out how simplistic much of our current approach to clinical diffusion-weighted imaging is at the moment, and how much room for future exploration remains. Diffusion imaging has become an essential part of clinical MR imaging, and it is difficult to imagine routine imaging without it. Nonetheless, we are on the threshold of an even higher level of complexity and understanding of diffusion-weighted imaging.

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The Status of Status: Seizures Are Bad for Your Brain's Health

What is the relationship between seizures and brain dysfunction? Because seizures and epilepsy represent symptoms of an underlying disorder, rather than the disorder itself, their relationship to cognitive function is variable. Although 0.5% to 1% of the population suffers from recurrent seizures, most lead productive lives. In some cases, abnormal cognitive function coincides with seizure activity because both represent different phenotypic displays of the underlying etiology, such as in diffuse developmental conditions like the agyria-pachygyria disorders. Cognitive impairment also occurs during and after the ictus, and may accompany treatment with antiepileptic drugs. Two important questions are raised: do seizures directly cause brain damage, and do they augment epileptogenicity? If seizures do cause progressive brain or epileptogenic dysfunction, then early intervention for seizure control is indicated in order to prevent further brain injury.

A number of experimental animal and clinical imaging studies support the idea that seizures by themselves cause brain damage (1). Experimental animal models have shown that intense limbic seizures result in a pattern of hippocampal damage similar to hippocampal sclerosis. Similar imaging changes have been reported in the human hippocampus after prolonged nonfebrile or febrile seizures; the hippocampus initially becomes enlarged and hyperintense, and then later atrophies. Several MR imaging studies have correlated hippocampal atrophy with duration of epilepsy. Gray matter volume has been negatively correlated with seizure duration, suggesting that neocortical changes may be a consequence of seizures. One study found that generalized seizures appear to cause progressive brain dysfunction in patients with temporal lobe epilepsy. Frequent generalized seizures were correlated with bilateral temporal lobe metabolic dysfunction by use of MR spectroscopy, and ipsilateral atrophy by use of MR volumetry.

When seizure activity is markedly prolonged, as in status epilepticus, brain damage can occur quickly and be profound. Histologic studies from both humans and animal models have shown that brain damage primarily affects the hippocampus, amygdala, and piriform cortex; the cerebral cortex, cerebellar cortex, and thalamus are affected to a lesser extent. MR imaging with long TRs have shown regional hyperintense changes that occur during or immediately after onset of seizure activity in humans with status epilepticus (2). These changes usually resolve with time, followed by regional atrophic changes.

Status epilepticus can also be evaluated by diffusion-weighted MR imaging and apparent diffusion coefficient (ADC) measurements (2, 3). Although a number of studies describe these rela-

tionships in detail, the reports by Men et al (a clinical case report, page 1837) and Wall et al (an animal study, page 1841) in the current issue of the *AJNR* enhance our knowledge by their wonderful correlation with histopathologic findings. While diffusion changes have been reported in humans with status epilepticus, there is a paucity of histopathologic correlation (2). With regard to animal models of status epilepticus, diffusion changes are well documented. Sequential, correlative diffusion-pathologic changes, however, have not been described for the first 24 hours after the onset of status epilepticus as provided by Wall et al. Correlative studies are imperative for us to understand what seizure-induced imaging findings truly represent, and in turn, the pathophysiology of this type of brain damage.

What is the current understanding of diffusion changes induced by status epilepticus? Transient decreases in ADC (and increased signal changes on diffusion-weighted images) are observed in regions of seizure activity, usually accompanied by hyperintense signal changes on long-TR images. The regions with decreased ADC correspond to regions of transient, increased perfusion and EEG abnormalities. The most affected regions are the amygdala, piriform cortex, and hippocampus. The cerebral cortex, cerebellar cortex, and thalamus are involved to a lesser extent. In animal models, decreases in ADC occur as early as 1 hour after status epilepticus, become most pronounced at about 24 hours, and then normalize over the next week (3). In humans, the time course is less well defined, but also appears to be transient. The diffusion changes, accompanied by signal changes on T2-weighted images, usually resolve when imaged weeks later and atrophy ensues. Hyperintense signal changes on long-TR images may persist, especially in the hippocampus and amygdala. These acute changes can be differentiated from those caused by stroke by using perfusion-weighted MR imaging techniques. Unlike in cases of stroke, there is a focal increase in regional cerebral blood volume and an increased mean transit time.

The diffusion changes appear to be due to seizure-induced changes in cellular membrane permeability and ion homeostasis, with a resulting elevation of extracellular potassium and an influx of sodium and calcium. Swelling of neurons and glial cells occurs as free water rapidly follows the osmotic gradient into the cells. ADC values are thought to increase because of the rapid shift of water from extracellular compartments to the more restrictive intracellular environment. T2 measurements are prolonged because of the increase in water content. Swelling of cells may lead to irreversible cellular edema, resulting in selective neuronal necrosis as described by Wall et al and Suleyman et al. As the cells lyse, ADC values normalize over time and MR imaging reveals atrophic changes

While there is now abundant evidence that status epilepticus is detrimental to brain tissue, and that diffusion-weighted imaging (and ADC maps) can document this damage, several questions remain. Does abnormal diffusion (and ADC values) always mean subsequent neuronal death? The answer appears to be no for the retrospenial cortex, according to Wall et al. Case reports of seizure-induced, transient diffusion changes without associated T2 changes may also represent cases of reversible cellular changes. What is the explanation for the ADC changes in the hippocampus in the study by Wall et al? The answer is not clear. ADC increases in the amygdala and piriform cortex in the pilocarpine model of status epilepticus as reported by Wall et al and the kainic acid model reported by others (3). However, Wall et al report a decrease in hippocampal ADC values, whereas those using the kainic acid model report an increase. The explanation provided by the authors does not appear to be sufficient.

Our understanding of the pathogenesis of seizures is still incomplete, but studies that correlate imaging findings with cellular microenvironment (like the reports in this journal) will help fill in the gaps.

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