

# Magnetic Resonance Imaging (MRI) in ALS: Is a “Normal” Scan Really All We Can Expect?

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ALS ultimately remains a clinical diagnosis, meaning that the physician must order and review the results of multiple tests and ultimately consider all of them in order to determine whether an individual does or does not have ALS. As most of you know, this can be a long and stressful process. In some patients undergoing evaluation for progressive weakening, the diagnosis is not clear, particularly early in the course of the disease, and may mimic other neurological processes. It is not unusual for patients to have undergone repeated and expensive laboratory, radiological, pathological, and electrodiagnostic evaluations, and perhaps even surgery, before the diagnosis of ALS is made. Clearly there is a need to develop better diagnostic tests for ALS.

Magnetic resonance imaging (MRI) is a powerful imaging technique which is used extensively in the diagnosis of such diverse processes as strokes, brain tumors, and multiple sclerosis, but has not played a major role in the diagnosis of ALS, other than serving to rule out other disorders. Thus, the MRI of the brain and spinal cord in individuals with ALS is often interpreted as “normal.” However, some new MRI techniques are beginning to show promise in assisting in the diagnosis of ALS in a more positive way, by showing findings that are abnormal in ALS. These MRI techniques include magnetic resonance spectroscopy (MRS), diffusion tensor imaging (DTI), and voxel-based morphometry (VBM). MRS evaluates target tissues by determining the ratio of three primary metabolites: n-acetylaspartate (NAA), choline (Cho), and creatine (Cr). A decreased NAA/Cr ratio (suggesting neuronal disruption) has been reported in ALS. MRS has also shown differences in NAA, NAA/Cr, NAA/Cho ratios between ALS patients and age-matched controls. DTI provides image contrast by evaluating the movement of water molecules. Regions of the nervous system known as the corticospinal tracts and the corpus callosum appear different in patients with ALS than in normal controls when studied by DTI. VBM uses advanced automated software to calculate precise volumes of specific brain regions of interest. Additionally, this technique allows one to determine if an interval change has occurred by allowing comparison of the identical brain region on examinations done at different times. VBM has proved useful in understanding Alzheimer’s Disease and has also been used to study frontotemporal dementia (which may occur in ALS, as discussed in one of my previous columns). Although such studies are in their infancy, a study of VBM in ALS has recently shown changes in the grey matter of some brain regions in patients with ALS. In addition to these novel techniques, MRI can be used to study iron deposition in the brain. We are very

interested in this because of our studies on mutations in the hemochromatosis (Hfe) gene and their relationship to ALS.

With this in mind, we are now undertaking a study to examine the relationships between Hfe gene mutation status, iron profiles, comprehensive cognitive testing (tests of thinking and concentration), and MRI data on a group of individuals with ALS and to follow changes over time. A number of our patients and some of their family members have agreed to participate in this study, and we are most grateful. This study, just recently begun, will evaluate 15 individuals with ALS and 15 neurologically normal controls. The MRI studies will be performed at 6 month intervals, using the novel techniques described above. One goal of the study is to seek to identify which MRI techniques may be useful in making the diagnosis of ALS. We also hope to learn more about which regions of the brain outside of the motor area, such as those areas involved in cognition, may show changes in ALS. In addition, by following individuals with ALS over time and repeating their scans at 6 month intervals, we hope to better understand how the changes in the brain evolve as the disease advances. Thus, we are hopeful that this study will not only lead to more rapid and accurate techniques for arriving at the diagnosis of ALS, but will also lead to a more complete understanding of the disease and its evolution over time. And, as new treatments are tried for ALS, we are hopeful that MRI scans done at regular intervals over the course of such treatments may help us to determine whether the treatments are working by altering the way in which ALS affects the brain over time. If our studies are successful, then a “normal” MRI may not be the finding expected when making the diagnosis of ALS.