Creutzfeldt-Jakob Disease: Comparative Analysis of MR Imaging Sequences

BACKGROUND AND PURPOSE: MR imaging has played an increasingly important role in the diagnosis of Creutzfeldt-Jakob disease (CJD) since basal ganglia abnormalities on T2-weighted images have been described; thus, the aim of our study was to compare the value of different MR images in the diagnosis of CJD.

METHODS: One hundred fifty-seven patients with CJD underwent MR imaging examinations. Ninety-two patients were neuropathologically confirmed, and 65 were clinically classified as having CJD through the CJD Surveillance Unit (probability of 95%). There was no standardized MR imaging protocol; thus, the examinations included 143 T2-weighted, 43 proton attenuation (PD)-weighted, 84 fluid-attenuated inversion recovery (FLAIR), and 44 diffusion-weighted images (DWI). The MR images were reviewed for pathologic changes of the basal ganglia, thalamus, and cerebral cortex.

RESULTS: Cortical abnormalities were present in 70 patients (45%) and were visible in 80% (35/44) of all available DWI examinations. The basal ganglia were affected in 94 patients (60%), in particular in the caudate nucleus; the most sensitive sequences were DWI (64%) and PD-weighted (63%). A thalamic involvement was more frequently diagnosed on PD-weighted images (19%) and DWI (14%) than on FLAIR or T2-weighted images.

CONCLUSION: PD-weighted images and DWI showed better results in the diagnosis of signal intensity changes in the basal ganglia compared with T2-weighted or FLAIR images; however, in the diagnosis of cortical changes, DWI was clearly superior. Our data suggest that DWI is the most sensitive MR imaging technique in the diagnosis of CJD.

Creutzfeldt-Jakob Disease (CJD), a fatal neurodegenerative disorder, is diagnosed by the detection of an accumulation of an abnormal form of the human prion protein PrPSc in the brain.1,2 Brain biopsy or autopsy is required for a definitive diagnosis (definite CJD).3 In sporadic CJD (sCJD), diagnostic MR examinations are performed frequently and reveal typical findings.4-7 Hyperintense signal-intensity abnormalities, initially reported on T2-weighted and proton attenuation (PD)-weighted images, were also detectable on fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted images (DWI): the signal intensity in the head of the caudate nucleus and in the putamen was compared with that in the thalamus and the cerebral cortex to distinguish normal gray matter intensity from pathologic hyperintensity. These changes have a reported sensitivity of 67% and a specificity of 93% for the diagnosis of CJD.5

The comparison of the MR imaging signals of the basal ganglia with those in the thalamus and the cortex has become more and more questionable because hyperintensities were also found in the thalamus and, in some cases, also in the cerebral cortex. With the application of other sequences, such as FLAIR and DWI, these signal intensity changes are more easily identifiable.8 DWI shows a decrease of the apparent diffusion coefficient (ADC) in the affected areas, most probably because of the characteristic neuropathologic spongiform neuropil changes.9-11

The purpose of our study was to identify the most sensitive MR imaging technique in determining signal intensity abnormalities in patients with sCJD.

Methods
All patients suspected of having CJD in Germany are reported to the Surveillance Unit (CJD-SU) in Goettingen. An experienced neurologist from the CJD-SU supports the on-site clinician, personally examines the patient on the spot, and collects copies of the electroencephalogram (EEG) and MR imaging examinations as well as specimens from CSF. Thus, MR imaging scans were collected from every relevant patient being reported to the CJD-SU.

We conducted a retrospective analysis of 199 consecutively referred patients with sCJD. At this time, no variant CJD (vCJD) case has been identified in Germany; our sample only consists of sCJD patients. The patients were classified as probable sCJD from 1999 to 2003.

The quality of the MR images was evaluated (1, excellent; 6, not diagnostic) before the scans were rated for pathologic signal intensity alterations on the different available sequences. Forty-two examinations were considered not diagnostic (eg, because of motion artifacts); a sufficient MR imaging quality was present in 157 scans (mean ± SD, 2.7 ± 1.1).

Because there was no standardized protocol, the examinations included 143 T2-weighted scans, 43 PD-weighted scans, 84 FLAIR scans, and 44 DWIs (Fig 1). The observations were documented separately for caudate nucleus (CN), putamen, thalamus, and cerebral cortex. The results were evaluated by using the χ² test.

Among the 157 patients, definite sCJD was proved by autopsy in 92 cases; in 65 patients, there was no consent for biopsy or autopsy by the patient or the patient’s family.
In 112 (71%) of the 157 patients, typical signal intensity alterations were present on MR imaging (Fig. 2).

**Cortex**

Abnormal signal intensity in the cortex (Fig 1) was found in 70 cases (45%). On FLAIR images, pathologic changes were diagnosed in 52% (44/84) and in 16% (7/43) on PD-weighted images. Findings on T2-weighted images were rated as abnormal in regard to cortical changes in only 6% (8/143). Cortical changes were most sensitively detectable on DWI: 80% (35/44) of the MR imaging examinations showed cortical areas with restricted water diffusibility, confirmed by ADC mapping (Fig 3).

In 17 cases, DWI was the only MR imaging technique showing the cortical pathology. Thus, in 39% of all patients whose examination included DWIs, the diagnosis was based exclusively on this technique.

**Basal Ganglia**

The basal ganglia (Fig 4) were involved in 94 patients (ie, 60% of all patients with CJD). In those cases with any abnormalities on MR imaging (112 patients), an abnormal signal intensity in the basal ganglia was found in 84%. The CN was affected most frequently (85 [90%] of the 94 patients with basal ganglia abnormalities). Putaminal involvement was found in 79 patients (84%), and 7 patients (7%) had an abnormal signal intensity in the pallidum. A singular pathology in just 1 of the nuclei was found in 24 cases (26%): 15 in the CN (16%) and 9 in the putamen (10%). A combination of CN involvement and putaminal involvement was detected in 63 patients (67%). An involvement of the pallidum was found only if both CN and putamen were affected as well.

Fifty-four percent (85/157) of the acquired MR imaging examinations presented abnormal signal intensities in the CN, but there was a big difference regarding the MR techniques. PD-weighted imaging and DWI detected these alterations significantly more frequent than T2-weighted images ($P < .01$): 64% (28/44) on DWI and 63% (27/43) on PD-weighted imaging compared with only 35% (50/143) on T2-weighted imaging.

Thirty-five percent (78/157) of the MR imaging examinations showed an abnormal signal intensity in the putamen, which was visible on T2-weighted images in 38% (54/143), whereas hyperintensities were detected in 58% (25/43) on PD-
weighted and in 37% (31/84) on FLAIR imaging. Findings of DWI were considered pathologic in 45% (20/44). Statistically, there was a significant difference between PD-weighted imaging on one side and T2-weighted and FLAIR imaging on the other side, indicating a higher sensitivity of PD-weighted imaging (P < .05). There was no significant difference between PD-weighted imaging and DWI.

**Discussion**

The clinical diagnosis of sCJD is based upon the combination of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of generalized periodic of rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of neurologic dysfunction. Additionally, generalized periodic sharp wave complexes (PSWC) in the EEG or the detection of general...
quences carry a higher risk of motion artifacts. DWI should be part of the MR imaging protocol in the examination of patients with dementia, especially if young patients are involved and/or the symptoms progress rapidly.

In addition to the protein 14–3–3 and EEG changes, MR imaging may be a helpful paraclinical tool and should be incorporated in the WHO diagnostic criteria for sCJD.

References