Temporoparietal Atrophy May Be AD Identifier

BY JEFF EVANS

BALTIMORE — Atrophy in the temporoparietal cortex might be a common identifier of Alzheimer's disease patients that differentiates individuals who have atypical clinical presentations of the disease from those who have other types of dementia, according to a small MRI scanning study.

Patients who have an atypical presentation of Alzheimer's disease (AD) but nonetheless have the amyloid-beta plaques and neurofibrillary tangles of tau protein that pathologically diagnose the disease have much less hippocampal atrophy than do patients who present with the typical clinical characteristics used to diagnose AD—loss of episodic memory, executive dysfunction, visuospatial and perceptual deficits, and language dysfunction, Dr. Keith A. Josephs said at the annual meeting of the American Neurological Association.

Patients who do not have those symptoms are usually diagnosed with a frontotemporal dementialike syndrome, progressive aphasia syndrome, or a corticobasal syndrome characterized by asymmetric, extrapyramidal, and cortical dysfunction. However, patients with those symptoms most frequently have a type of frontotemporal lobar degeneration (FTLD), such as FTLD with the deposition of TAR-DNA binding protein-43 (TDP-43), corticobasal degeneration pathology, Pick's disease pathology, or progressive supranuclear palsy pathology.

Differentiating AD from other dementias is important if future treatments for AD differ from FTLD, "which is likely, given the fact that the proteins that are deposited in Alzheimer's disease differ from the ones in FTLD," said Dr. Josephs of the department of neurology at the Mayo Clinic, Rochester, Minn.

To predict AD pathology in patients who present with a range of atypical AD clinical syndromes, Dr. Josephs and his colleagues looked at the gross structure of the brain with volumetric MR imaging rather than by imaging amyloid-beta or tau proteins.

They found 14 patients at the Mayo Clinic in Rochester who had a diagnosis of atypical AD dementia. These patients were evaluated by a behavioral neurologist and determined not to have a typical presentation of AD but were pathologically confirmed to have a high-probability diagnosis of AD according to National Institute on Aging–Reagan Institute Consensus Conference criteria (Braak stage V or VI). They also had at least one volumetric MRI scan.

Of the 14 patients with atypical AD, 6 had aphasic dementia, 5 had a corticobasal syndrome, and 3 had a clinical diagnosis of behavioral-variant frontotemporal degeneration. Dr. Josephs and his associates compared the atypical AD patients with 14 patients with pathologically diagnosed FTLD who had the same clinical dementia syndromes.

They also compared the atypical AD patients with 14 patients who had both the typical clinical symptoms and pathological signs of AD and 20 healthy control patients.

In each group, patients had a mean age of about 64 years at disease onset with a mean of 3.4 years from disease onset to the time of the MRI scan. Half of the patients in each group were women.

The typical AD patients showed the expected areas of atrophy in the temporoparietal cortex and hippocampi. However, atypical AD patients had temporoparietal atrophy but no hippocampal atrophy. FTLD patients had anterior-temporal, some posterior-frontal, and hippocampal atrophy.

In comparisons between the groups, both typical AD and FTLD patients had more hippocampal atrophy than did atypical AD patients. The atypical AD patients showed more putamenal atrophy than did typical AD patients. The atypical AD patients also had more temporoparietal atrophy than did the FTLD patients.

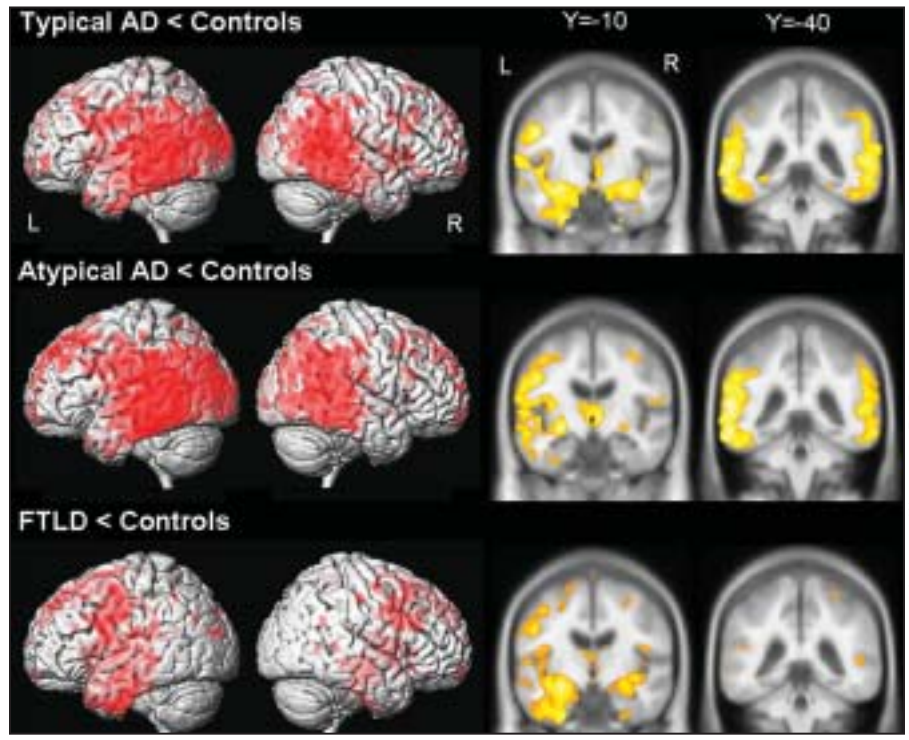
Patterns of atrophy also tended to vary across the dementia syndrome subtypes found among the atypical AD patients when compared with the healthy control patients, but all of the atypical AD patients had temporoparietal atrophy in common.

In individual analyses of each patient, typical AD and FTLD patients had significantly more hippocampal atrophy than did individual atypical AD patients.

However, individuals with either typical or atypical AD had significantly more temporoparietal atrophy than did FTLD patients. The pattern of atrophy was not driven by one specific clinical dementia subtype.

"Temporoparietal atrophy may be a signature of Alzheimer's disease independent of syndromic presentation. … Hippocampal atrophy does not appear to be at least an early prominent feature of atypical Alzheimer's disease. Later on, 5-6 years down the road, as the process progresses and there's degeneration, well, you might find hippocampal atrophy then," Dr. Josephs said.

The study was funded by grants from the National Institutes of Health and the Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program of the Mayo Foundation. Dr. Josephs had no disclosures to report. ■



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The medial temporal lobes are relatively spared in atypical Alzheimer's disease, compared with typical AD and frontotemporal lobar degeneration.

New Imaging Techniques Show Longer-Term Effects of TBI

BY MICHELE SULLIVAN

BANGKOK, THAILAND — New imaging techniques might help to explain the disabling symptoms that can plague patients with traumatic brain injury long after their acute problems have resolved, and eventually guide the best choice for medical therapy, Dr. Ramon Diaz-Arrastia said at the World Congress of Neurology.

Imaging techniques that are now well established in other areas of neurology—such as diffusion-weighted and susceptibility-weighted MR imaging—are now being used to show that brain injuries leave permanent, life-altering marks behind after the contusions and hematomas have healed.

These findings might have both immediate and long-range benefits, said Dr. Diaz-Arrastia, a professor of neurology at the University of Texas Southwestern Medical Center, Dallas.

In the future, imaging the post-TBI brain might help guide medical treatment choices and monitor drugs' effectiveness.

So far, nearly 30 drugs have provided effective neuroprotection in animal models of TBI, he said. However, none that has undergone testing in well-designed phase III trials has proven beneficial to humans.

Part of the problem might be the heterogeneity of human brain injury, Dr. Diaz-Arrastia said. There are many subtypes of TBI, yet "from the point of view of the clinical trials, all patients who present in a coma [after a brain injury] are treated the same way, even though the injuries can be very different, with very different prognoses."

Susceptibility-weighted imaging (SWI) is one technique being studied in TBI patients. It measures the paramagnetic shift of intravascular deoxyhemoglobin and methemoglobin, amplifying the appearance of microhemorrhages and making them much easier to identify. "SWI picks up 640% more lesions and 200% more lesion volume than does gradient-recall echo," Dr. Diaz-Arrastia said, referring to work by Dr. Karen Tong from Loma Linda (Calif.) University.

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DR. DIAZ-ARRASTIA

SWI is very good at identifying diffuse microvascular injury, a marker for diffuse axonal injury that is usually invisible on computed axial tomography. "The only problem is that SWI may be overly sensitive," he said.

Diffusion-weighted imaging (DWI), which is well established in the stroke world, is understudied in TBI, probably because it's a challenge to perform magnetic resonance imaging on these acutely ill patients. But this technique provides detailed information about the makeup of lesions.

Diffusion tensor imaging shows how water tracks along the axons, giving a good view of white matter lesions. Follow-up scans on TBI patients have shown tantalizing clues to the possible causes of their long-term problems.

Another technique moving into trauma field is quantitative volumetric assessment of the cortical field. "We have found that the brain shrinks overall after a severe traumatic injury, but that not all structures shrink at the same rate. Some cortical regions shrink very little, while others appear particularly sensitive to injury." This finding makes sense given the cognitive and mood issues that TBI patients can experience, he said. ■