Posterior cortical dementia
Lost but not forgetting
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As we approach the centennial of Alois Alzheimer's seminal contributions to neurology, our patients remind us that we often lose track of his important observations. Alzheimer described a diverse syndrome with a prominent memory disorder and a variety of cortical findings. In this issue of Neurology, Renner et al.1 and Tang-Wai et al.2 shed new light on the syndrome of posterior cortical dementia, first described in the 1980s as a visuospatial harbinger of Alzheimer disease (AD).3,4

Both groups report a syndrome of posterior cortical deficits in patients who are somewhat younger than most demented persons. Renner et al. describe 27 patients (mean age 66 years) who presented with visuospatial signs and symptoms that were at least as prominent as memory impairment. The most common visuospatial disturbances included elements of Balint's syndrome (ocular apraxia, optic ataxia, simultagnosia) and Gerstmann's syndrome (acalculia, agraphia, finger agnosia, right-left confusion). Posterior cortical neighborhood findings included language impairments, especially subtle non-fluency, and apraxia, especially of the ideomotor variety.

Tang-Wai et al. describe 40 patients (mean age = 60) who presented with elements of Balint's syndrome, especially simultagnosia, or of Gerstmann's syndrome, especially acalculia. Visual field defects were common, as were ideomotor apraxia and anosmia. Notably, memory and insight were well preserved: no memory complaints were reported and the patients provided intuitive descriptions of their deficits.

Both groups of investigators note an array of higher-order visual defects that stand out as the most distinguishing feature of posterior cortical dementia. Three of the four patients detailed by Renner et al. had navigational disorders and six of the patients studied by Tang-Wai et al. had symptoms characterized as environmental disorientation. Such complaints have long been recognized as being typical of patients with occipito-parietal lesions.5 In AD, it is becoming lost in familiar surroundings that commonly forces patients to give up driving and independent living.

Some patients had prominent visual recognition deficits. One patient was unable to recognize her own image in the mirror.1 Others complained of trouble seeing objects in clutter, words in text, and landmarks in their surroundings.2 These problems are typical of patients with occipito-temporal lesions.6 In AD, such deficits are related to the commonly encountered increasing effortfulness of reading, a substantial loss of a lifelong pleasure in many of these patients.

The dual, parallel nature of visual deficits in these cases corresponds to Kleist's dichotomizing of extrastriate visual function into two domains: an occipito-parietal domain devoted to visual localization and an occipito-temporal domain devoted to visual recognition.7 These domains correspond to the dorsal-ventral dichotomy of visual function that has emerged from experimental studies.8 Laboratory investigations show that dorsal extrastriate parietal cortex contains neurons specialized for orientation and navigation9 and ventral extrastriate temporal cortex contains neurons specialized for object characterization and identification.10

Both parietal and temporal extrastriate cortices contain discrete functional modules demonstrated by experimental microlocalization studies. In posterior cortical dementia, the discrete impairments that form the elements of classically defined neurobehavioral syndromes reveal this modular architecture. Neurodegeneration, however, presents those symptoms in diverse combinations different from the etymologically identified syndromic combinations derived chiefly from stroke neurology and reflecting,
perhaps, the interaction of microlocalization with patterns of cerebral perfusion.

The underlying pathologic processes of posterior cortical dementia are diverse. However, Alzheimer's changes were present in most of the cases from both Renner et al. (76%, 16/21) and Tang-Wai et al. (78%, 7/9). Lewy bodies were also seen in three of the cases from Renner et al. and two from Tang-Wai et al. Two patients from each series who developed parkinsonian features proved to have corticobasal degeneration. In the series from Renner et al., two additional patients showed evidence of prion disease; one had Creutzfeldt-Jakob disease and the other had fatal familial insomnia.

Gross pathologic changes were not needed to define the syndrome of posterior cortical dementia. Tang-Wai et al. required CT or MR evidence of posterior cortical atrophy for entry into their study. Renner et al. based enrollment of patients on neurologic criteria; of their patients, 24 later underwent CT or MR imaging. Only two showed posterior cortical atrophy.

Micropathologic analyses performed by Tang-Wai et al. revealed a pattern in posterior cortical dementia distinct from that of AD in patients who did not have prominent cortical findings. The posterior cortical group showed a surprising paucity of Alzheimer's changes in the hippocampus and adjacent subiculum. Rather, they showed unusually large numbers of neurofibrillary tangles, but not senile plaques, in striate visual cortical area 17 and extrastriate area 18. The posterior cortical group also showed evidence of retrograde degeneration in the lateral geniculate nucleus. Two conclusions are warranted: first, there is a syndrome of early onset dementia presenting with posterior cortical deficits, most prominently visual and visuospatial impairments, with relatively preserved memory. It is noteworthy that language and praxis deficits are common neighborhood findings in these patients. Second, this syndrome most often represents the selective development of Alzheimer's pathologic alteration in striate and extrastriate visual cortex with relative sparing of mesial temporal structures.

The presence of alternative pathologic processes in only 20 to 25% of the cases makes persons with a diagnosis of posterior cortical dementia relatively more homogenous than an otherwise unrestricted population of persons with late-life dementia, about half of whom show pathologic processes other than those of AD.

As a variant of AD, posterior cortical dementia raises several fundamental questions. Is the conventional sequence of Braak stages, representing spread from mesial temporal lobe to convexity cortex, fundamental to the disease or just one of many patterns of degeneration? If phenotypic variants of AD begin outside of mesial temporal structures, might they reflect distinct genotypic variants? Alternatively, might such phenotypic variants represent the interaction of a genotypic propensity to Alzheimer's changes with functional stressors predisposing to earlier manifestations at different locations in the brain?

In studying dementia we must be mindful of the diverse presentations noted by Alzheimer and the lessons gleaned from the intervening century of syndromic behavioral neurology. Analyzing diverse impairments may lead to inferences about pathophysiology, predictions about behavioral vulnerability, and the specific therapies anxiously awaited by all who are touched by this illness.

References