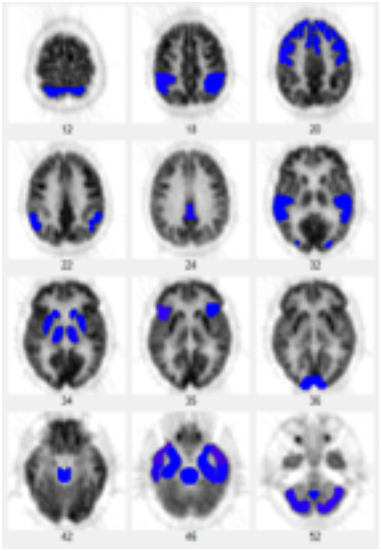
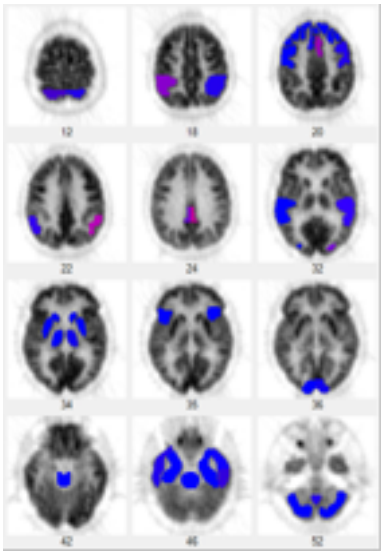
Description of Example Patient's

Demo, Case1 – Normal Case

This case demonstrates the quantitative output produced by NeuroQ™ when it is used to analyze a normal study. The blue areas within the cluster regions indicate that the metabolic uptake was all above the normal limit of 1.65 standard deviation. Mr. E was 71 years old when he was first referred to the UCLA Ahmanson.



Demo, Case2 – Mildly Abnormal



Patient History

Mr. E was 71 years old when he was first referred to the UCLA Ahmanson Biological Imaging Division in December 2001 with concern for worsening memory. He reported that he always had a poor memory, but that over the preceding seven years, he began to notice his memory getting worse, including forgetting where he put his keys and forgetting names or faces. Mr. E had worked as a physicist for 25 years and taught physics at the University-level for the following 20 years. He reported no psychiatric hospitalizations, illness, or medication use. Mr. E had no significant medical history, including hospitalizations or illness, with the exception of prostate surgery for benign enlargement. He did not use tobacco, alcohol or other drugs and had no history of such use. His physical examination, neurologic exam and blood laboratory values (including TSH, B12, CBC, ALT and Cr) were within normal limits. Mr. E underwent comprehensive neuropsychologic testing at the time of his first visit in 2001, and was found to be cognitively normal for his age.

Why was a PET scan obtained at this time?

This patient is seeking a diagnosis for his chief complaint, a convincing history of cognitive decline. His symptoms are unexplained by any factors identified in his history, physical or laboratory work-up. Moreover, for patients possessing his apparent high level of pre-morbid intellectual ability and education, it is common for loss of cognitive ability to be experienced, while still being able to perform at levels considered to be within the normal ranges of standard neuropsychological tests.

PET Interpretation

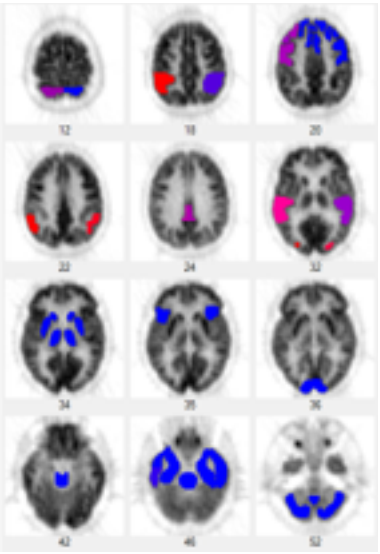
The scans from 2001 and 2004 each reveal mild parietal/temporal hypometabolism, more pronounced on the left (right side of image). NeuroQ™ analysis identifies mild abnormalities (purple to red shades) in parietal/temporal and posterior cingulate regions, with well-preserved metabolism in other regions (blue shades)… a pattern very suggestive of early Alzheimer's type changes occurring in this patient's brain.
The pattern of cerebral metabolism in 2004 has slightly changed since 2001. Visually, there appears to be slight interim worsening of parietal/temporal hypometabolism. [Show combined figure with arrows, on slide 3, here.] That impression is bolstered by the NeuroQ™ analysis, which shows in its plane 22 image the left parietotemporal cortex advancing to a near-red shade (12% and 4 standard deviations below normal) in 2004, from the purple shade (9% and 3 SD below normal) seen in 2001.

Case Summary

To summarize, at a time when conventional clinical evaluation was not sufficiently sensitive to document cognitive abnormality in this 71 year old physicist reporting memory problems, PET was already documentably (mildly) abnormal, both by visual and quantitative analyses. From 2001 to 2004, neuropsychologic performance with respect to immediate and delayed memory for word associations, contextual information, rote list learning, and complex visual stimuli declined across testing sessions, indicating "significant cognitive deterioration" within those abilities, according to the neuropsychologist. By 2004, Mr. E's performance met criteria for "Mild Cognitive Impairment," performing between one and two standard deviations below the mean established for his same age peers on at least 50% of the memory tasks. The combination of this clinical progression, with the posterior-predominant pattern of hypometabolism affecting especially parietal/temporal cortex is most consistent with the presence of incipient Alzheimer's disease. Armed with the FDG-PET information, his managing physician prescribed an anti-Alzheimer's combination regimen including both donepezil and memantine in advance of the second neuropsychologic testing session. On his current regimen, he continues to achieve 30/30 on the Mini Mental State Examination (MMSE).

Demo, Case3 – Severely Abnormal

Patient History



Mr. F was 63 years old when he underwent FDG-PET in August 1996 for symptoms of decreased memory, language and visual skills. The cognitive decline had been noted for at least 2 years, as had been sensory and motor deficits of his left upper extremity. Mr. F's past medical history was positive for pyelonephritis, prostatitis, and prostate surgery for benign enlargement. The patient had a history of heavy alcohol use in the past, but had discontinued drinking, and did not use tobacco or other drugs nor have a history of such use. He was a lawyer, as was his wife, and they had two small children. His physical examination, other than his neurologic exam was normal. His neurologist noted upon exam that the patient got two of three items correct regarding orientation and three of four words remembered correctly at 3 minutes, and that he had marked apraxia of the upper extremities with left worse than right, plus "mild Parkinsonism with a mask face"; cranial nerves were intact and reflexes were normal. Blood laboratory tests obtained one month prior to PET were normal, including CBC, electrolytes, BUN, creatinine, glucose, calcium, cholesterol, and liver enzymes; VDRL and TSH tests obtained the following year were also normal. The neurologist following Mr. F, an internationally recognized expert on dementia and Director of a university-based Alzheimer's Disease Center, diagnosed him with corticobasal degeneration and depression, for which he was treated with the antidepressant sertraline.

Structural Neuroimaging

1992 Brain MRI revealed "mild enlargement of the lateral ventricles… otherwise unremarkable."
1994 Brain MRI with and without contrast revealed "progression of cerebral atrophy."
1995 Brain MRI revealed "moderate generalized cerebral atrophy which is not significantly changed when compared to the scan of 1994. The scan is otherwise within normal limits."
1996 Brain MRI with and without contrast revealed "stable appearance of cerebral cortical atrophy."
1997 Head CT revealed "cerebral atrophy but is otherwise negative."

Why should the patient get a PET scan at this point in his evaluation?

Mr. F has documented cognitive decline and motor symptoms noted on neurologic examination. The symptoms are unexplained by his general history, physical examination, laboratory screen and structural neuroimaging tests, which are largely unremarkable. Although he was evaluated by a prominent dementia expert who did not suspect Alzheimer's disease, there are no tests (short of brain biopsy) documented to be as accurate as FDG-PET in the identification of Alzheimer's disease that the neurologist did, nor could do, to exclude the possibility of that now-treatable condition.

Clinical Follow-up

Mr. F. continued to progressively deteriorate with respect to cognitive and motor symptoms, also developing a seizure disorder before his death that proved resistant to medical therapy. An autopsy was performed in 2000 at the Alzheimer's Disease Center for which the patient's neurologist was Director, and the final diagnosis was "Alzheimer disease, [Braak and Braak Stage VI, CERAD definite]" with abundant neurofibrillary tangles in the hippocampus, entorhinal cortex and neocortex, as well as amyloid-beta(1-42)-staining plaques prominent throughout all areas of hippocampus, entorhinal cortex and neocortex. (Synuclein staining to check for the presence of Lewy bodies was not performed.)

Case Summary

To summarize, by the time of this PET scan, Mr. F. had undergone extensive evaluation of his cognitive and motor symptoms, including history and physical examinations by his internist, neurologic examination by a dementia expert, laboratory screening, as well as multiple brain MRI studies, two of them including contrast, and

subsequently a head CT. The clinical examination led to diagnoses of corticobasal degeneration and depression, the laboratory screen was negative, and the structural imaging studies demonstrated only atrophy.
None of the above studies pointed to the presence of Alzheimer's disease, and the patient correspondingly received no treatment specific to that diagnosis. The presence of Alzheimer's disease, however, was clearly evident on both PET and autopsy examinations. PET also revealed profound hypometabolism of associative visual cortex (quantified by NeuroQ™ as falling as much as 12 standard deviations below normal metabolic levels) suggesting Lewy body involvement, which could also help to explain the prominence of the patient's central motor symptoms.

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