Optics tests for early Alzheimer's diagnosis make significant advances

October 3 2006

Providing an update on progress and new findings on his optical tests for the early detection of Alzheimer's disease, Lee Goldstein of Brigham and Women's Hospital and Harvard Medical School will describe dramatic new developments in the technology during a plenary talk at Frontiers in Optics, the annual meeting of the Optical Society of America (OSA) in Rochester, N.Y., which takes place next week.

At the plenary talk, Goldstein will present "proof of concept" evidence obtained in mice that the tests can detect early molecular signs of the disease in the eye even before Alzheimer's pathology is present in the brain. This achievement raises hopes for detecting the disease at its earliest stages and slowing the progression of the disease to a crawl.

Goldstein envisions that the tests could become part of a suite of "universal early screening technologies" that would be a routine part of an annual physical exam for people starting in middle age. With the tests, envisioned to be relatively inexpensive, physicians would be able to monitor patients year to year for any signs that the disease is present and progressing. The goal, according to Goldstein, is to catch the disease early in its course when treatment is likely to be most effective.

The technology may have additional value in accelerating clinical testing of new emerging treatments for the disease.

At last year's annual OSA meeting, Goldstein unveiled two laser-based eye tests that could detect unusual cataracts composed of the amyloid

beta protein, the same molecules that are the hallmark of Alzheimer's disease. Previously, Goldstein and his colleagues had discovered evidence that Alzheimer's was not just a brain disease, but rather a "systemic" one that manifests itself in the lens of the eye. The amyloid beta proteins that form plaques in the brain and impair cognitive function also build up near the edge of lens, ultimately forming an unusual "supranuclear" cataract that is very different from more familiar, age-related cataracts.

Fortunately, Goldstein says, the only pathological molecules that seem to form in this particular part of the lens are the amyloid beta particles, tremendously simplifying the researcher's task of differentiating Alzheimer's from other disease states involving the lens. "Mother Nature dealt us a lucky hand here," he says.

Both of the optical tests involve the use of a low-intensity laser that very briefly is directed into the lens, shining low-power light into the eye. The light is safe and barely visible to the patient and does not provide any discomfort, Goldstein says.

In the first test, light enters the lens and ricochets or "scatters" from tiny particles too small for the eye to see. The "quasi-elastic" light scattering test can detect small clumps of beta-amyloid particles in the lens. The beta-amyloid proteins collect as aggregates in the lens as small as tens to hundreds of nanometers in size. Small increases in the size or number of these nanometer-scale particles create large effects in light scattering that are detected and analyzed by the technology, he says.

Recently, Goldstein and his colleagues have shown in animal trials that this test can detect the particles that form the unusual cataract associated with Alzheimer's disease, but even before they coalesce into something that can be seen with the naked eye.

"We can pick this up in entirely clear lenses," Goldstein says. "This is exactly what we want to be doing."

The second test uses eye drops that contain a specially designed "ligand" that specifically binds to amyloid beta proteins. When laser light from the instrument is directed into the lens, the amyloid then emits a characteristic light signal that is detected and analyzed by the technology. Goldstein emphasizes that these are not imaging tests--the output of the technology is not a picture to be read like a chest X-ray--but rather a "molecular diagnostic" that can detect and analyze suspicious amyloid beta deposits in the lens.

Recently, Goldstein and his colleagues showed in mice that they could pick up signs of the protein in the lens even before the classic amyloid brain lesion of Alzheimer's disease developed in the brain. This is vitally important, he says, as early detection is the only way that physicians can effectively treat the disease. In addition, detecting Alzheimer's early through eye tests can monitor the effectiveness of the many drugs being developed to slow the condition.

Meanwhile, these techniques have been tested in a Phase I trial in humans with phase III multicenter human clinical trials slated for next year. In the end, the tests could cost less than $300 per test, he says. As a potential early screening tool and confirmatory diagnostic technology, this is the ballpark range for a widely used test, he says. As no definitive test for diagnosing Alzheimer's currently exists, the tests may also help to differentiate the earliest stages of Alzheimer's from other neurodegenerative diseases and normal changes in cognition associated with aging.

So the eyes may be more than a poet's window to the soul. They may also be a gateway to the brain and to effective early treatment of a devastating brain disorder. The Alzheimer's disease research of

Goldstein and his team is funded by the National Institutes of Health, American Federation for Aging Research, Alzheimer's Association, and the American Health Assistance Foundation. Goldstein is a co-founder and scientific consultant to Neuroptix Corporation, a Massachusetts-based diagnostic biotechnology company that has licensed and is developing the technology for clinical use.

Source: Optical Society of America