MedicalXpress

Alzheimer's disease: Simplified diagnosis, with more reliable criteria

July 7 2014

How many patients receive an incorrect diagnosis of Alzheimer's disease? The answer is a surprisingly high number: over a third! To reduce the number of errors, the diagnostic criteria must be the most reliable possible, especially at the very early stages of the disease. For the last decade, an international team of neurologists, coordinated by Bruno Dubois (Inserm/Pierre and Marie Curie University/AP-HP Joint Research Unit 975) has been working towards this. In the June issue of *The Lancet Neurology* journal, we see how the researchers have developed a simplified diagnosis based on the most specific criteria of the disease. A challenge primarily for research, but also for clinical practice.

Alzheimer's disease is a neurodegenerative disease. It is the most common (70%) form of dementia. In France, the number of people with Alzheimer's disease and other forms of dementia is estimated at between 750,000 and one million, and is expected to reach 1.29-1.40 million patients by 2030. Alzheimer's disease results from a loss of neurons. The lesions are caused by an accumulation of some brain proteins. The pathology begins with memory problems. This is followed by problems of orientation in space and in time, behavioural problems and loss of autonomy. However, these symptoms are not specific to Alzheimer's disease. The real challenge is to know how to distinguish this disease from other types of dementia, and establish the diagnosis as reliably and as early as possible.

In 2005, an international group of neurologists, coordinated by Bruno

Dubois at Inserm, came together to redefine the diagnostic criteria established in 1984. Until then, it had been necessary to await the death of a patient in order to establish a diagnosis of Alzheimer's disease with certainty by examining the lesions in his/her brain. And in the living, only a probability of disease could be inferred, and only at a late stage, based on a certain threshold of severity of dementia.

In 2007, the international team shattered these concepts. The researchers introduced new diagnostic criteria, particularly biomarkers. These are genuine signatures of the disease, and are present from the initial symptoms (prodromal stage).

The publication of these results constituted a revolution. Researchers then observed that with these new criteria, "36% of their patients included in a therapeutic trial based on previous clinical criteria did not have Alzheimer's disease," reports Bruno Dubois. And although this analysis involved only a subgroup of patients, the implications are serious. Patients did not receive the correct treatment and/or care. And flawed patient selection might have had an impact on the lack of efficacy observed for the new treatment.

Since 2007, many studies have been published. And the international group decided to analyse this literature to make the diagnostic algorithm for Alzheimer's disease simpler and more reliable.

"We have reached the end of the road; we have arrived at the essence, something refined, resulting from an international consensus", indicates Prof. Dubois. The diagnosis of Alzheimer's disease will henceforth rely on "just a couple of clinical-biological criteria for all stages of the disease" (see box).

Most of the time, the diagnosis of Alzheimer's disease is based primarily on a suggestive clinical picture. It is subsequently confirmed or rejected

using a biomarker.

As regards the clinical picture, there are three scenarios:

- typical cases (80-85% of all cases): impairment of episodic long-term memory (known as amnestic syndrome of the hippocampal type and corresponding to difficulty remembering a list a words, even with clues, for example)
- atypical cases (15-20% of cases): atrophy of the posterior part of the cerebral cortex or logopenic aphasia (impairment of verbal memory where the patient inverts the syllables of a word when repeating it, for example), or frontal brain damage (which results in behavioural problems)
- preclinical states: asymptomatic at-risk (patients without symptoms, but who are fortuitously discovered to have positive biomarkers during scientific studies), and presymptomatic (with a genetic mutation)

One of the following two biomarkers is required:

- in the cerebrospinal fluid (obtained by lumbar puncture): abnormal levels of brain proteins (reduced beta amyloid protein and increased tau protein)
- in the brain by PET (positron emission tomography) neuroimaging: elevated retention of amyloid tracer

This simpler and more reliable algorithm is important, primarily for research (therapeutic trials, characterisation of the disease, monitoring of patient cohorts, etc.). Outside of research, the use of biomarkers, which is expensive and/or invasive, currently remains limited to young patients or difficult or complex cases in expert centres.

More information: Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria, *The Lancet Neurology*, vol.13, juin 2014. www.thelancet.com/journals/lan … rticle/PIIS1474-4422%2814%2970090-0/fulltext