

# IR spectroscopy method is promising for clinical test that could detect Alzheimer's early

03/17/2016

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Recognizing that current Alzheimer's disease diagnosis methods only address symptomatic treatment, researchers at Ruhr University Bochum (RUB; Germany) and collaborators at the University of Göttingen and the German Center for Neurodegenerative Diseases (DZNE; Göttingen, Germany) have developed a clinical test based on immunochemical analysis using infrared (IR)-induced difference spectroscopy that may lead to early detection of Alzheimer's.

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The promising test involves an IR sensor, whose surface is coated with highly specific antibodies that extract biomarkers for Alzheimer's from the blood or the cerebrospinal fluid taken from the lower part of the back (lumbar liquor). The IR sensor then performs spectroscopic analysis to determine if the biomarkers show already pathological changes, which can take place more than 15 years before any clinical symptoms appear.

"If we wish to have a drug at our disposal that can significantly inhibit the progress of the disease, we need blood tests that detect Alzheimer's in its pre-dementia stages," says Prof. Dr. Klaus Gerwert, Head of the Department of Biophysics at RUB. "By applying such drugs at an early stage, we could prevent dementia, or at the very least delay its onset," adds Prof. Dr. med. Jens Wiltfang, Head of the Department for Psychiatry and Psychotherapy at the University of Göttingen and Clinical Research Coordinator at DZNE Göttingen.

For the test, the secondary structure of beta amyloid (A $\beta$ ) peptides serves as a biomarker. This structure changes in Alzheimer's patients. In the misfolded, pathological structure, more and more A $\beta$  peptides can accumulate, gradually forming visible plaque deposits in the brain that are typical for Alzheimer's disease. This, as mentioned previously, happens more than 15 years before first clinical symptoms are present. The pathological A $\beta$  plaques can be temporarily detected by positron emission tomography (PET), but this procedure is comparatively expensive and is accompanied by radiation exposure.

The IR sensor developed by the research team that detects misfolding of A $\beta$  peptides involves extracting the A $\beta$  peptide from body fluids. After initially working with cerebrospinal fluid, the researchers subsequently expanded the method towards blood analysis. "We do not merely select one single possible folding arrangement of the peptide; rather, we detect how all existing A $\beta$  secondary structures are distributed, in their healthy and in their pathological forms," says Gerwert. Precise diagnostics is not possible until the distribution of all secondary structures is evaluated. Tests that analyze A $\beta$  peptide are already available with enzyme-linked immunosorbent assays (ELISA). They identify the total concentration, percentage of forms of different length, as well as the concentration of individual conformations in body fluids, but they do not provide information on the diagnostically relevant distribution of the secondary structures at once. "This is why ELISA tests have not been proven very effective when applied in blood sample analysis in practice," he explains.

The research team used the new method to analyze samples from 141 patients, achieving diagnostic precision of 84% in the blood and 90% in cerebrospinal fluid. The test revealed an increase of misfolded biomarkers as spectral shift of A $\beta$  band below threshold, allowing the researchers to determine Alzheimer's.

Currently, sample analyses for early detection in 800 study participants are being conducted to optimize statistical significance.

Details of the work appear in the *Journal of Biophotonics* and in the journal *Analytical Chemistry*.