Physicist reports binary marker of preclinical and clinical Alzheimer's disease

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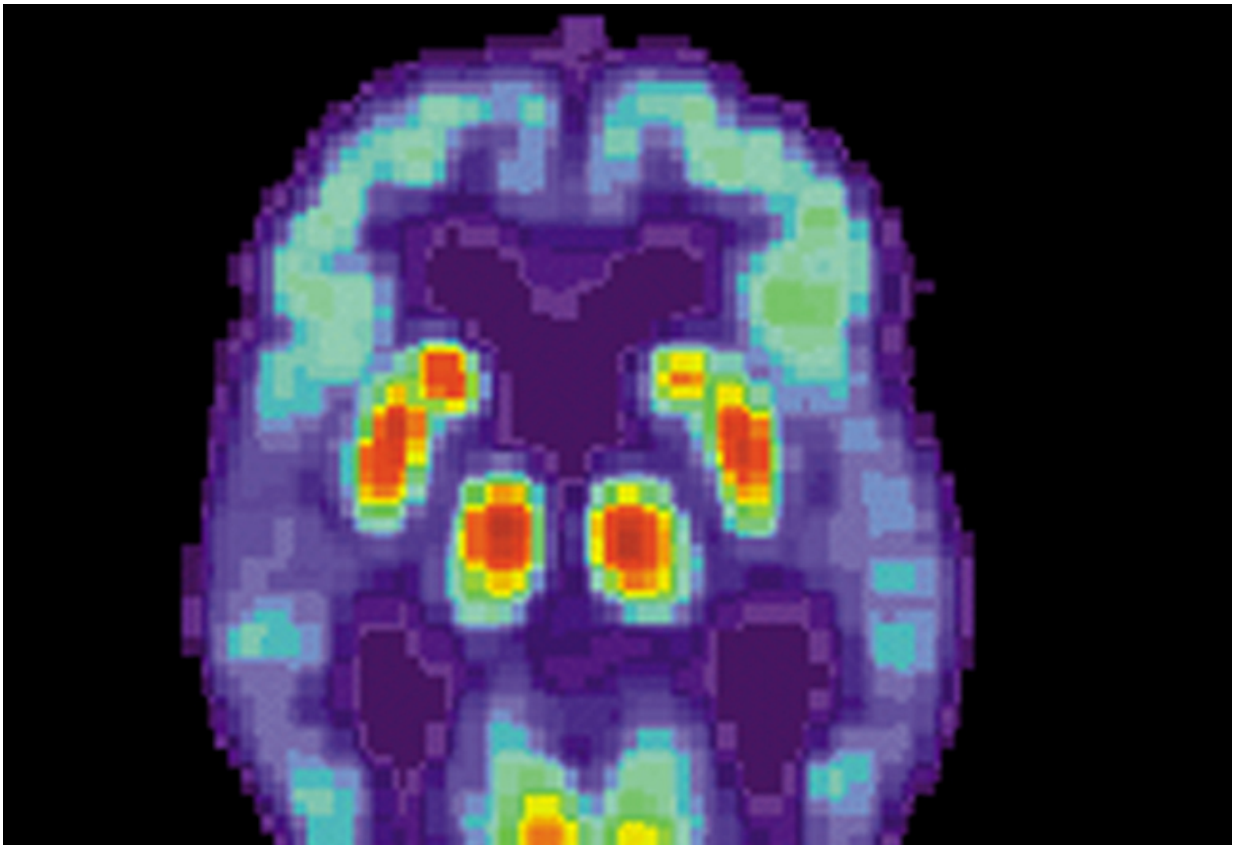

PET scan of a human brain with Alzheimer's disease. Credit: public domain

A new technique shows high potential for providing a discrete, non-invasive biomarker of Alzheimer's disease (AD) at the individual level during both preclinical and clinical stages. The proposed biomarker has a

large effect size (0.9) and high accuracy, sensitivity and specificity (100 percent) in identifying symptomatic AD patients within a research sample, according to Sanja Josef Golubić Ph.D. of the University of Zagreb. She is the leading author of a new study published in the neuroimaging journal *Human Brain Mapping*.

"Ultra-weak neuromagnetic fields were acquired with a whole-head MEG system inside a two-layer magnetically shielded room, while anatomical data were obtained from T1-weighted and T-2 weighted turbo spin echo magnetic resonance images from a 1.5-T MR scanner at the Mind Research Network in Albuquerque, New Mexico," says Golubić. "To localize cortical sources of the extracranially measured fields evoked by an auditory oddball paradigm, we modeled neural generators assuming multiple current dipoles embedded in a spherical volume conductor. We conducted spatio-temporal source localization during the entire 100 ms post-stimulus time window. Estimation of the time invariant parameters (spatial locations) was derived using nonlinear minimization and kept constant for the selected time window, while a linear estimation of the associated time varying parameters (source strengths and orientation) were calculated for each time instance."

The medial prefrontal cortex and the bilateral supratemporal areas were identified as cortical regions where the gating network were localized. The three different gating generator topologies were found across subjects and two conditions based on the activation of a prefrontal generator.

Golubić says, "The symptomatic AD patients were lacking any medial prefrontal gating generator activations to either the deviant or standard tones of a paradigm. To the contrary, high functional controls activated prefrontal generator in response to both paradigm tones. We also detected a sub-group of controls characterized by the absence of prefrontal gating generator activation for the standard tone only and

significantly lower scores at the Mini Mental Status Exam and delayed Rey-Osterreith Complex Figure Test. We speculate that these individuals may be in a possible preclinical AD phase since they show both neuropsychological and neurophysiological impairments characteristic for an AD type of dementia, although they did not yet meet clinical criteria for early phase of symptomatic AD."

"Our non-invasive AD biomarker does not require estimation of cut-off levels or standardization processes what is the main problem with so far proposed AD markers. Its strength lies in the simplicity of using a binary value i.e. activated or not-activated prefrontal sensory gating generator. The low sensitivity to individual heterogeneity and variability due to the binary nature of impaired medial prefrontal generator activation is probably the most important property of the proposed biomarker," says Josef Golubić.

The discovery is a highly promising AD marker at the individual level. However, this approach needs to be further tested in a large independent sample and requires assessment in longitudinal clinical studies.

More information: Sanja Josef Golubic et al. MEG biomarker of Alzheimer's disease: Absence of a prefrontal generator during auditory sensory gating, *Human Brain Mapping* (2017). DOI: 10.1002/hbm.23724

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