# Research blog for March

- **Cognitive Difficulties Can Predict Neurodegeneration, Study Finds**

A set of "objectively-defined subtle cognitive difficulties," termed Obj-SCD, has been identified in previous research, and can be used to classify patients during the early stages of Alzheimer's.

People classified as having Obj-SCD may have overall assessment scores in the normal range but the way in which they complete the tasks given in testing may have recognizable errors.

Having Obj-SCD has been shown to predict faster progression to mild cognitive impairment, or MCI, and dementia, in comparison with those who are classified as cognitively normal. Obj-SCD also has been associated with the presence of biomarkers for Alzheimer's present in the cerebrospinal fluid (CSF), the liquid that surrounds the brain and spinal cord.

Now, the researchers wanted to understand whether Obj-SCD occurs before or after amyloid starts to accumulate, and whether it can be used to predict future amyloid accumulation and neurodegeneration.

The team found that amyloid accumulation was faster in participants classified as having Obj-SCD than in the cognitively normal group. Additionally, it was shown that Obj-SCD can be identified before or at the same time as the early phase of amyloid accumulation. The cognitive difficulties also could predict the progression to MCI and dementia.

These findings suggest that measurements of mild cognitive impairment may be a sensitive and noninvasive predictor of neurodegeneration.

**Source:**
**https://alzheimersnewstoday.com/2020/02/28/alzheimers-disease-subtle-cognitive-difficulties-can-predict-amyloid-accumulation-neurodegeneration/**

- **DNA from Bacteria in Brain May Promote Tau Clumping, Study Suggests**

Alzheimer's is characterized by the formation of amyloid plaques and tau tangles in the brain, which disrupt communication between nerve cells and cause their death.

Researchers at the Human Microbiology Institute (HMI), a nonprofit research group, and the Mitchell Center for Alzheimer's disease at the University of Texas McGovern Medical School in Houston looked at what happens to the tau protein when extracellular DNA from different species of bacteria is present.

The study involved mixing normal tau with extracellular DNA from bacteria — including *Pseudomonas aeruginosa*, *Tetzosporium hominis*, *Tetzerella alzheimeri*, *Escherichia or E. coli*, *Porphyromonas gingivalis*, and *Borrelia burgdorferi* — and culturing them in those same conditions.

The team found that several, but not all, bacterial species promoted tau clumping. The bacteria that accelerated the process the most were *T. alzheimeri*, and *E. coli,* while *P. gingivalis* and *B. burgdorferi* had only a moderate effect at promoting clumping. They also tested DNA from *Candida* – a fungus also found in the central nervous system of some patients — and human cells for comparison. These had a much lower promoting effect than extracellular bacterial DNA.

The researchers believe that they may have found a principally new lead not only for treating Alzheimer's, but also for its prevention.

**Source:**
**https://alzheimersnewstoday.com/2020/02/26/bacterial-dna-may-promote-tau-clumps-in-brain-study-suggests/**

- **Evidence on Cognitive Impairment Screening in Older Adults Is Insufficient, Panel Says**

Should adults older than 65 be screened for cognitive impairment if they are asymptomatic? Not necessarily, according to a US Preventive Services Task Force (USPSTF) recommendation statement, which suggested that the current evidence is insufficient to recommend whether cognitive impairment screening should be used to assess community-dwelling, asymptomatic older adults.

The recommendation, published on February 25, 2020 in *JAMA*, serves as an update to the 2014 recommendation by the USPSTF. The task force had requested a review of the literature on cognitive impairment screening, including mild to moderate dementia and mild cognitive impairment among asymptomatic, community-dwelling adults older than 65. The new statement is consistent with the 2014 USPSTF recommendation.

The panel based its recommendation on a review of published research through January 2019. The review included evidence on the harms and benefits of interventions and

treatment for older adults with cognitive impairment and their caregivers and the accuracy of screenings in identifying cognitive impairment.

Although the studies reviewed do not collectively offer strong support for screening for treatment or cognitive impairment of cognitive deficits, the lack of evidence in the existing literature does not mean that screening is not beneficial at all, the editorialists noted.

Clinicians should be aware of early symptoms or signs of cognitive impairment, like problems with language or memory, and evaluate patients accordingly, they added. Clinicians can recommend these approaches to reduce risk to all older adults without the need for any cognitive screening.

The American Academy of Neurology suggests using validated, brief cognitive assessment instruments to evaluate for cognitive impairment and has established guidance for detecting cognitive impairment during yearly wellness visits.

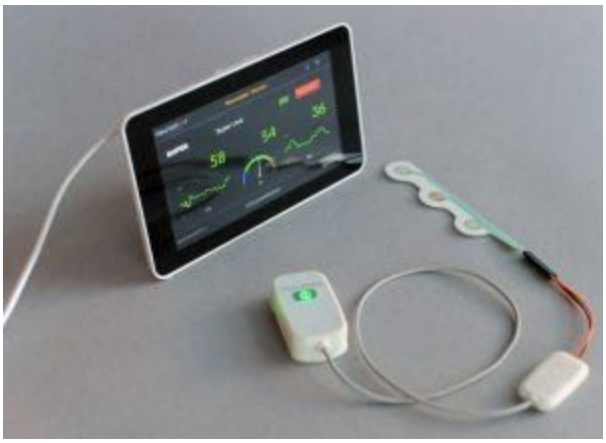
**Source:**
**https://journals.lww.com/neurotodayonline/blog/breakingnews/pages/post.aspx?PostID=905**

- **Neurosteer Promotes Wearable Monitor to Detect Early Alzheimer's**

Within a few years, doctors will be able to remotely evaluate patients for their risk of developing Alzheimer's disease, Parkinson's disease and frontotemporal dementia — without having to hook them up to expensive, cumbersome machines generally found only in hospitals. That's the vision of Israeli entrepreneur Nathan Intrator, CEO of Neurosteer.

Current EEG monitors, to assess the electrical activity of the brain, are quite large, containing between 16 and 256 electrodes.

Intrator founded Neurosteer in 2015, and has since developed a wearable device that consists of only three electrodes. The adhesive EEG sensor strip is placed on a patient's forehead. It's essentially a battery-powered amplifier and an analog-to-digital converter, with Bluetooth capability to send the signal to the cloud using proprietary algorithms.



Neurosteer three-electrode strip and monitoring screen.

Neurosteer uses signal processing, artificial intelligence, and machine learning to produce high-level biomarkers linked to various brain states and neurological disorders.

The units themselves will sell for a few thousand dollars each, and will be manufactured in the U.S., Europe, and potentially Israel. Neurosteer is currently conducting clinical trials in the United States as well as Belgium, Israel, Italy, and Britain.

Neurosteer's market for the new product includes pharmaceutical companies, as well as patients who arrive at hospital emergency rooms with stroke, epilepsy, or traumatic brain injuries.

**Source:**
**https://alzheimersnewstoday.com/2020/03/10/neurosteer-promotes-wearable-monitor-to-detect-early-alzheimers/**

- **PSEN1 Gene Alteration May Be Early Biomarker for Alzheimer's, Study Suggests**

A specific chemical alteration, called DNA methylation , present in the presenilin1 (*PSEN1*) gene may be a biomarker for earlier Alzheimer's disease (AD) diagnosis and treatment response monitoring, a study suggests.

The alteration was observed both in brain samples of Alzheimer's mouse models and post-mortem brain tissue of Alzheimer's patients. It was also measurable in blood samples from patients with late-onset AD, suggesting its detection is a new, non-invasive way to diagnose the illness.

The researchers found that *PSEN1* gene was over-expressed in the post-mortem brain human samples of Alzheimer's patients. In both sexes, there was a significant inverse relationship between the levels of gene expression and DNA methylation.

The levels of *PSEN1* methylation in the blood were significantly lower in Alzheimer's patients than in controls. This "opens the door to developing this assay as a potential biomarker for the disease," the researchers wrote. Furthermore, lower PSEN1-related methylation levels corresponded to increased *PSEN1* activity.

The researchers said, further studies in a larger cohort using DNA from blood and post-mortem brain tissue obtained from the same individuals [are necessary] to validate this potential biomarker. If found to be causal, these findings would provide a starting point for developing epigenetic therapies.

**Source:**
**https://alzheimersnewstoday.com/2020/03/16/psen1-gene-alteration-may-be-early-biomarker-for-alzheimers-study-suggests/**

- **Stress-Related Disorders Are Associated with Increased Risk of Neurodegenerative Disease**

People with stress-related disorders had an increased risk of neurodegenerative diseases compared with individuals who were not subject to psychiatric reactions induced by trauma or other life stressors, according to a population-matched and sibling cohort study published in *JAMA Neurology* on March 9.

The increased risk was more pronounced for vascular disease—at 80 percent—than for other primary neurodegenerative diseases—at 31 percent, reported Huan Song, MD, PhD, of West China Hospital in Chengdu, China, and colleagues.

Prior research on the general population and male veterans has shown that posttraumatic stress disorder is linked with increased risk of dementia. One investigation with limited control for familial factors also supported the link between dementia and all stress-related disorders, the investigators noted.

The researchers did not find a statistically significant association between stress-disorders and amyotrophic lateral sclerosis or Parkinson's disease. However, the association was significant for Alzheimer disease.

**Source:**
**https://journals.lww.com/neurotodayonline/blog/breakingnews/pages/post.aspx?PostID=910**

- **Blood Test Can Differentiate Alzheimer's From Other Dementias, Research Suggests**

A blood test that measures the levels of a form of tau protein, known as phosphorylated-tau-181 (pTau181), could help diagnose Alzheimer's disease in patients who show signs of dementia but have an uncertain diagnosis, a study suggests.

Currently, two techniques are used to differentiate Alzheimer's from other dementias: brain imaging, specifically to visualize amyloid-beta deposition in the brain using positron emission tomography (PET), and cerebrospinal fluid (CSF) testing to measure the levels of amyloid and tau protein. Both techniques, however, present significant downsides, such as invasiveness, high cost, and exposure to radiation.

In the study, a team of researchers at the University of California (UC) measured the concentration of pTau181 in the blood plasma of more than 400 participants from the UC San Francisco's Memory and Aging Center (part of the Alzheimer's Disease Research Centers), the Advancing Research and Treatment for Frontotemporal Lobar Degeneration consortium, as well as a research study sponsored by Eli Lilly.

The team observed that Alzheimer's patients had blood plasma levels of pTau181 that were 3.5 times higher than were found in those with Frontotemporal Dementia, differentiating these groups from each other as well as Alzheimer's patients from healthy controls.

Importantly, this blood test was able to identify participants who were positive for amyloid-beta brain depositions as observed with PET imaging, regardless of their clinical diagnosis, and correlated with the levels of tau deposition in the brain.

**Source:**
**https://alzheimersnewstoday.com/2020/03/09/blood-test-can-differentiate-alzheimers-from-other-dementias-research-suggests/**

- How and Why Living in Disadvantaged Communities Contributes to Neurodegeneration

Where a person lives may be one of the social factors that can influence their brain health, suggests a new imaging study of older residents from urban and rural neighborhoods in Wisconsin. The neighborhoods were considered socioeconomically

disadvantaged based on a measure that factors in income, education, employment, and housing quality in characterizing a neighborhood.

The paper, published January 6 online in *JAMA Neurology*, found older residents of the most disadvantaged neighborhoods had smaller hippocampal areas and total brain volume than their peers in less disadvantaged neighborhoods. However, the study authors acknowledged that the presence of cardiovascular disease factors such as obesity, hypertension, and cholesterol played a role in driving the loss of total brain volume.

Hippocampal and cortical volume loss precedes clinically-identifiable cognitive deficits, said study author Barbara Bendlin, PhD, associate professor at the University of Wisconsin-Madison School of Medicine and Public Health and Wisconsin Alzheimer's Disease Research Center (ADRC).

The impact of neighborhood disadvantage on hippocampal volume was equivalent to the loss expected to be seen with an additional seven years of aging, said Dr. Bendlin.

The study is part of a larger research program that is examining a wide-range of factors that contribute to aging brain health or pathology being conducted at the Bendlin Laboratory at the University of Wisconsin and funded by the National Institute on Aging.

**Source:**
**https://journals.lww.com/neurotodayonline/Fulltext/2020/03050/How_and_Why_Living_in_Disadvantaged_Communities.5.aspx**