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Machine learning gives nuanced view of Alzheimer's stages

By David Nutt, Cornell Chronicle

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A Cornell-led collaboration used machine learning to pinpoint the most accurate means, and timelines, for anticipating the advancement of Alzheimer's disease in people who are either cognitively normal or experiencing mild cognitive impairment.

The modeling showed that predicting the future decline into dementia for individuals with mild cognitive impairment is easier and more accurate than it is for cognitively normal, or asymptomatic, individuals. At the same time, the researchers found that the predictions for cognitively normal subjects is less accurate for longer time horizons, but for individuals with mild cognitive impairment, the opposite is true.

The modeling also demonstrated that magnetic resonance imaging (MRI) is a useful prognostic tool for people in both stages, whereas tools that track molecular biomarkers, such as positron emission tomography (PET) scans, are more useful for people experiencing mild cognitive impairment.

The team's paper, "**Machine Learning Based Multi-Modal Prediction of Future Decline Toward Alzheimer's Disease: An Empirical Study** (https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0277322)," published Nov. 16 in PLOS ONE. The lead author is Batuhan Karaman, a doctoral student in the field of electrical and computer engineering.

Alzheimer's disease can take years, sometimes decades, to progress before a person exhibits symptoms. Once diagnosed, some individuals decline rapidly but others can live with mild symptoms for years, which makes forecasting the rate of the disease's advancement a challenge.

"When we can confidently say someone has dementia, it is too late. A lot of damage has already happened to the brain, and it's irreversible damage," said senior author **Mert Sabuncu** (https://sabuncu.engineering.cornell.edu/), associate professor of electrical and computer engineering in the College of Engineering and Cornell Tech, and of electrical engineering in radiology at Weill Cornell Medicine.

“We really need to be able to catch Alzheimer’s disease early on,” Sabuncu said, “and be able to tell who’s going to progress fast and who’s going to progress slower, so that we can stratify the different risk groups and be able to deploy whatever treatment options we have.”

Clinicians often focus on a single “time horizon” – usually three or five years – to predict Alzheimer’s progression in a patient. The timeframe can seem arbitrary, according to Sabuncu, whose lab specializes in analysis of biomedical data – particularly imaging data, with an emphasis on neuroscience and neurology.

Sabuncu and Karaman partnered with longtime collaborator and co-author Elizabeth Mormino of Stanford University to use neural-network machine learning that could analyze five years’ worth of data about individuals who were either cognitively normal or had mild cognitive impairment. The data, captured in a study by the Alzheimer’s Disease Neuroimaging Initiative, encompassed everything from an individual’s genetic history to PET and MRI scans.

“What we were really interested in is, can we look at these data and tell whether a person will progress in upcoming years ?” Sabuncu said. “And importantly, can we do a better job in forecasting when we combine all the follow-up datapoints we have on individual subjects?”

The researchers discovered several notable patterns. For example, predicting a person will move from being asymptomatic to exhibiting mild symptoms is much easier for a time horizon of one year, compared to five years. However, predicting if someone will decline from mild cognitive impairment into Alzheimer’s dementia is most accurate on a longer timeline, with the “sweet spot” being about four years.

“This could tell us something about the underlying disease mechanism, and how temporally it is evolving, but that’s something we haven’t probed yet,” Sabuncu said.

Regarding the effectiveness of different types of data, the modeling showed that MRI scans are most informative for asymptomatic cases and are particularly helpful for predicting if someone’s going to develop symptoms over the next three years, but less helpful for forecasting for people with mild cognitive impairment. Once a patient has developed mild cognitive impairment, PET scans, which measure certain molecular markers such as the proteins amyloid and tau, appear to be more effective.

One advantage of the machine learning approach is that neural networks are flexible enough that they can function despite missing data, such as patients who may have skipped an MRI or PET scan.

In future work, Sabuncu plans to modify the modeling further so that it can process complete imaging or genomic data, rather than just summary measurements, to harvest more information that will boost predictive accuracy.

The research was supported by the National Institutes of Health National Library of Medicine and National Institute on Aging, and the National Science Foundation.

Many Weill Cornell Medicine physicians and scientists maintain relationships and collaborate with external organizations to foster scientific innovation and provide expert guidance. The institution makes these disclosures public to ensure transparency. For this information, see profile for ***Dr. Sabuncu*** *(https://vivo.weill.cornell.edu/display/cwid-mrs4002).*

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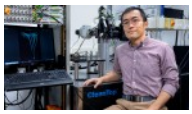

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