ALZHEIMER DISEASE

Penalized regression can predict conversion to AD

A new study has used multivariate regression analysis to determine which imaging biomarkers are most helpful for identifying patients with mild cognitive impairment (MCI) who are at risk of converting to Alzheimer disease (AD).

“With an increasing number of available imaging modalities for studies of AD, the problem of best biomarker selection is becoming a serious concern,” explains lead author Stefan Teipel.

Past studies have identified factors that predict AD via stepwise regression, where the most highly correlated data are added to a predictive model, and poorly correlated data are removed. According to Teipel, this stepwise approach can yield models that are ‘overfitted’: very accurate in one study, but poorly generalizable and not biologically plausible.

Teipel’s team analysed data collected as part of the Alzheimer’s Disease Neuroimaging Initiative, which included structural MRI, amyloid-PET (using the AV45 radioisotope) and ¹⁸F-FDG-PET scans from patients with MCI. The

investigators separated the participants into those who did and those who did not convert to AD after ~18 months ($n=39$ and $n=88$, respectively).

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Patients who converted to AD showed changes in grey matter volume, amyloid deposition and glucose metabolism in multiple regions compared with those who did not develop AD. When the investigators applied a conventional stepwise regression model to these data, they were able to predict AD with 66% accuracy using between 12 and 27 variables from the baseline scans.

Although this level of accuracy was encouraging, the factors highlighted by the model made little biological sense: for example, amyloid deposition in the right amygdala increased the risk of conversion while deposition in the left amygdala seemed to be protective against AD.

Teipel and colleagues, therefore, used a penalized regression technique, whereby each variable’s contribution to the model was limited by how much unique information it provided. This approach yielded slightly more-accurate predictions (72%) with only three to nine variables. The most predictive factor was PET-visible amyloid deposition in various cortical regions, including the posterior cingulate, temporal lobe and occipital lobe.

Teipel explains that the findings might offer a way to parsimoniously and efficiently predict conversion in patients with MCI. “This possibility will become particularly relevant when we bring current advances in imaging biomarkers from research into clinical care,” he says.

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Original article Teipel, S. J. *et al.* The relative importance of imaging markers for the prediction of Alzheimer’s disease dementia in mild cognitive impairment—beyond classical regression. *Neuroimage Clin.* doi:10.1016/j.nicl.2015.05.006