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Modeling Multivariate Age-related Brain Imaging Variables with Dependence: an application to assess the smoking effects on white matter tracts during brain aging

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Neuroimaging techniques have been increasingly used to measure the structures and functions of the aging brain. The imaging variables from distinct brain locations and modalities exhibit various trajectories along age reflecting the localized aging effects. Statistical challenges remain to model the multivariate imaging features while taking into account both the dependence structure and non-linear age trajectories. We propose a new mixed-effects model to study the association among dependent multivariate imaging variables, age, and other clinical covariates. We develop computationally efficient algorithms for parameter estimation. We show that our method can provide a better fit with a reduced root mean square error and improved inference efficiency by extensive simulation studies. We further apply our approach to UK Biobank data to investigate the effects of tobacco smoking on the whole-brain white matter integrity measures while adjusting the aging effect. We also identify the adverse effect of smoking on white matter integrity.