Hierarchical Linear Modeling of longitudinal Magnetic Resonance Spectroscopic Imaging

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Introduction

A comprehensive analysis of biomedical longitudinal data demands accommodation of between-subjects and within-subject variation, unbalanced designs and missing data. The longitudinal spectroscopic imaging data even complicate the problem by its large sources of variability. The goal of this study is to apply linear mixed models in the assessment of the change of 2 metabolites during short-term recovery from alcohol dependence and compare the results using different random effect model.

Materials and Methods

Multi-slice short-echo time ^{1}H MRSI was used to measure longitudinal changes in common brain metabolites in 81 subjects (65 recovering alcoholics (RA) and 16 light drinkers (LD) at 1.5 T. RA were studied at three time points (approximate 7, 35 and 200 days) and LD at two time points (approximate 7 and 200 days). Two metabolites, NAA (N-acetylaspartate) and Choline from the white matter of parietal lobe were used for this study.

A bivariate linear mixed model with random effects process and independent measurement error for both metabolites were used based on the following rationale.

Assume that errors from different subjects are uncorrected, a general linear model [1]

$$y_{ij} = \mu_{ij} + e_{ij}$$

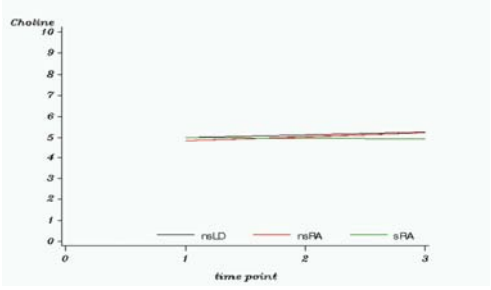
where y_{ij} (i = 1, 2, ….N; j =1,2,…m_i) be the continuous random variable corresponding the metabolites observed on the ith subject at the jth spectroscopic study, can become a generalization of the Larid and Ware model [2] by including correlation among within-subject errors

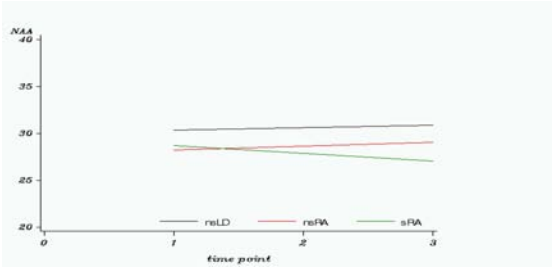
$$Y_i = X_i \beta + C_i \tau_i + W_i + e_i$$

where X_i and C_i is a design matrix for the fixed effect (β) and individual random effects (τ_i). W_i is a first order auto-regressive (AR) process for within-subject errors. The covariance function of the bivariate auto-regressive process w_i is given by $R_i = C * e^{B|t-s|}$ with C the covariance matrix at t=s and B is 2 by 2 matrix [3]. Univariate and bivariate random effect models were compared using likelihood ratio test.

Results

Fig.1. shows a predicted mean change of Choline (left) and NAA (right) at three time points of 3 study groups in the parietal white mater using bivariate random model with 2 random slopes. The bivariate random effects model was significantly better than univariate random effects model (-95373 vs. -100977, likelihood ratio).





nsLD: non-smoking light drinker, nsRA : non-smoking recovering alcoholics, sRA: smoking recovering alcoholics

Discussion

Hierarchical mixed model is useful in the evaluation of longitudinal change of spectroscopic metabolite data. The correlation structure of repeated measures between individual slopes for each response in the longitudinal spectroscopic imaging can be estimated using bivariate random model effect.

References

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[3] Thiebaut et. al., Computer Methods and Programs in Biomedicine 2002; 69:249