Title	Gene mapping of familial amyotrophic lateral sclerosis
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NUS-11 Gene mapping of familial amyotrophic lateral sclerosis

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Introduction: Amyotrophic lateral sclerosis (ALS) is a lethal neurodegenerative disorder characterized by gradual death of motor neurons in cerebral cortex, brain stem, and spinal cord. The pathogenetic mechanism remains unclear for the vast majority of cases. About 10% of ALS cases are familial (FALS). Cu/Zn superoxide dismutase (SOD1) gene accounts for about 10% of autosomal dominant FALS and the gene(s) responsible for the rest of ALS/FALS remain(s) to be found.
Method: We recruited a large Chinese kindred without SOD1 mutation for linkage analysis. Peripheral blood samples were collected and DNA were extracted from peripheral lymphocyte. We screened the family with ~ 400 polymorphic microsatellite markers. The genotyping data were subjected to model-based and model-free linkage analysis.
Result: Using MLINK of LINKAGE (Ver 5.2) package, we found a maximum LOD score of 4.357, $?_{[m=f]}$=0.0 at a microsatellite marker located at distal long arm of chromosome 8. Multipoint analysis by GENEHUNTER (Ver 1.2) revealed a maximum multipoint LOD score of 3.909 and NPL score 9.209. Haplotype analyses revealed a critical region which spanned 10.18-cM on chromosome 8.
Conclusion: We identified a 10.18-cM critical FALS region on chromosome 8. Further analyses using positional cloning and candidate gene approach are indicated to delineate the underlying genetic defect for FALS in this family.
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NUS-12 Magnetic resonance imaging and diffusion tensor imaging in Chinese neonates with hypoxic ischemic encephalopathy

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Introduction: Several studies have suggested the potential utility of diffusion tensor imaging (DTI) in the evaluation of brain injury in the asphyxiated neonates.
Method: We present our initial experience with DTI in Chinese neonates (gestational age 37 to 41 weeks, age 1 to 9 days of which there were 3 females) who were diagnosed as having hypoxic injury on clinical examination and the severity of the insult was graded using Apgar scores and Sarnat staging. Magnetic resonance imaging (MRI) with DTI was performed in eighteen neonates (eight with hypoxic ischemic encephalopathy [HIE] and ten with no cerebral pathology). The specific areas of interest were chosen in selected white matter (WM) areas: the posterior limb of the internal capsule, frontal WM, occipital WM, central WM, and temporal WM. The apparent/average diffusion coefficient (AADC) and relative anisotropy (RA) were compared between neonates with HIE and those without cerebral pathology using One-Way ANOVA.
Results: Abnormality on MRI was noticed in 3 of 8 neonates with HIE of different clinical stages. One neonate in Sarnat stage I and Apgar score of 10 showed periventricular changes as the MRI abnormality. Of the 2 neonates in Sarnat stage II and Apgar score of 3, one had periventricular changes and another showed thalamic abnormality. In contrast, DTI abnormality was noticed in all 8 neonates. A marked decrease of the AADC values was found in the posterior limb of the internal capsule, frontal WM and occipital WM in neonates with HIE. In addition, the RA values were marked reduced in HIE-affected neonates over the frontal WM and occipital WM.
Conclusion: The lower AADC in the capsule indicates active myelination and the presence of myelin, while the lower RA in the cerebral WM (e.g. frontal WM and occipital WM) over the site of injury indicates reduced directionality of diffusion in these brain areas and suggests that central fiber tracts have been destroyed or their subsequent development would be impaired. Based on our initial experience, we conclude that the DTI is potentially useful in understanding the basis of the neurologic deficits and DTI has a better correlation with the Sarnat staging and Apgar scores than MR imaging.