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THEME 6 EPIDEMIOLOGY

P145 CYANOTOXIN EXPOSURE AS A RISK FACTOR FOR SPORADIC ALS AMONG GULF WAR VETERANS

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Keywords: BMAA, cyanobacteria, cyanotoxins

Background: Epidemiological analysis of ALS cases among personnel deployed to the Gulf between 1990–1991 indicates a significant increase for post-war risk of sporadic ALS with incidence occurring at an earlier age than expected (1, 2). A time-limited outbreak of sporadic ALS occurred in the following decade, which is consistent with latent development of disease after exposure to environmental toxins (3, 4). A meta-analysis of 22 studies indicates increased sporadic ALS incidence in veterans of the Gulf War and of other military deployments (5). This search for a cosmopolitan etiological agent that could account for such exposures during various deployments has focused on β-N-methylamino-L-alanine (BMAA), a motor neuron toxin produced by cyanobacteria (6, 7).

Objectives: To determine if vehicular disturbance of cyanobacterial crusts during military activities within deserts of the Gulf could result in exposure of deployed personnel to BMAA through inhalation.

Methods: Cyanobacterial crusts were collected in the deserts of Qatar. Cyanobacterial taxa were identified and analyzed for BMAA using an Amino Acid Analyzer (AAA), Ultra Performance Liquid Chromatography/Mass Spectroscopy (UPLC/MS) and triple quadrupole Liquid Chromatography/Mass Spectroscopy/Mass Spectroscopy (LC/MS/MS). Crusts were artificially aerosolized to simulate vehicular disturbance and the dust analyzed using these methods.

Results: Gulf desert crusts were found to be rich in cyanobacterial genera including Chroococcus, Microcoleus and other species of the Oscillatoriaceae and contained BMAA according to AAA, UPLC/MS and LC/MS/MS analyses. Microcystin was identified through immunological assays and 2,4 diaminobutyric acid (DAB) was also detected in cultured material.

Discussion and Conclusions: Desert dust clouds are effective vectors of toxins from microorganisms (8, 9). Military deployment from 1991-1993 in the Gulf region resulted in significant dust due to vehicular disturbance and other military activities. Exposure of deployed personnel to BMAA, DAB and microcystins may have occurred from inhalation of aerosolized cyanobacterial crusts which may have contributed to the observed increased incidence of sporadic ALS. Cyanobacterial and cyanotoxin exposures through inhalation of dust or ingestion of contaminated water may also account for observed increases of sporadic ALS in other military deployments.

References:
1. Horner RD, Feussner JR, Hoff-Lindquist J *et al.* Neurology 2003; 61:742–749
2. Haley RW. Neurology 2003; 61:750–756
3. Horner RD, Grambow SC, Coffman CJ *et al.* Neuroepidemiology 2008; 31:28–32
4. Murch SJ, Cox PA, Banack SA. PNAS 2004; 101: 12228–12231
5. Rose MR, Brix KA. Phil Tran R Soc B 2006; 361:605–618
6. Liu XQ, Rush T, Zapata J *et al.* Exp Neu 2009; in press
7. Cox PA, Banack SA, Murch SJ *et al.* PNAS 2005; 102:5074–5078
8. Griffen DW. Clinical Microbiology Reviews 2007; 20: 459–477
9. Fleming LE, Kirkpatrick B, Backer LC *et al.* Environ Health Perspect 2005; 113:650–657

P146 A SPATIAL ANALYSIS OF ALS IN NEW ENGLAND: RELATIONSHIP TO TOXIC CYANOBACTERIA BLOOMS

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Keywords: cyanobacteria, epidemiology

Background: The incidence of Amyotrophic Lateral Sclerosis (ALS) is approximately two per 100,000 persons. An environmental factor which triggers sporadic ALS is supported by geographic disparities in the incidence of ALS and by the development of the disease in conjugal couples. A high incidence of Amyotrophic Lateral Sclerosis/Parkinsonism Dementia Complex (ALS-PDC) has been documented amongst the Chamorro people of Guam and the cyanobacteria toxin beta-methylamino-L-alanine (BMAA), found in components of the Chamorro diet, has been implicated. A high incidence of ALS in Enfield, New Hampshire, which encompasses a lake with a history of documented cyanobacteria blooms, has previously been reported. Exposure to cyanobacteria and cyanotoxins such as BMAA could occur through ingestion of water, consumption of contaminated fish, or inhalation of aerosolized cyanotoxins. Though a number of exposures could be shared by persons in a lakeside community, persons living within close proximity to cyanobacteria blooms may be more likely to be exposed to cyanotoxins and thus may be at a higher risk of developing ALS.

Objectives: To determine if persons living in close proximity to cyanobacteria blooms have a higher incidence of ALS.

Methods: Electronic records and community databases were reviewed to identify the dwelling addresses of patients presenting with ALS between 1998 and April 2009 in New Hampshire (NH), Vermont (VT) and Maine (ME). Case density was adjusted to account for the underlying population density using U.S. Census 2000 data. Records of recent algal blooms were obtained from each individual state's records. ArcGIS 9.3 software was used for spatial analysis. The incidence of ALS over a 10-year interval was calculated within a 0.5 mile (805 meter) buffer zone around

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lakes with documented blooms. This was then compared to the incidence of ALS for persons living farther than 0.5 miles from lakes with cyanobacteria blooms.

Results: Dwelling addresses were obtained for 553 cases of ALS in NH, VT and ME. The odds ratio of developing ALS for persons living within 0.5 miles of a lake with cyanobacterial blooms, compared to the odds for persons living outside this area, was 2.32 in NH (95% CI 1.42–3.80), 1.6 in VT (95% CI 0.9–3.2) and 2.77 in ME (95% CI 1.78–4.31).

Discussion: There appears to be an association between living in close proximity to New England lakes with cyanobacteria blooms and the development of ALS. Limitations of this study include the small number of cases, accuracy of dwelling addresses and the difficulty of retrospectively analyzing environmental factors related to a chronic, progressive disease. It is biologically plausible that exposure of a susceptible individual to a cyanobacterial neurotoxin such as BMAA could result in the development of ALS, however, causation cannot be inferred from a spatial association. Further studies are needed to examine the chronic effects of cyanotoxins.

P147 ESSENTIAL MINERALS AND RISK OF AMYOTROPHIC LATERAL SCLEROSIS ON THE KII PENINSULA, JAPAN

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Keywords: essential minerals, Kii-ALS, risk

Background: Previous epidemiological research in an area of the Kii Peninsula with a high-incidence of ALS (K area) demonstrated low concentrations of Calcium (Ca) and Magnesium (Mg) and high concentrations of toxic minerals, such as Manganese (Mn) or Aluminium (Al) in drinking water and soil compared to those in control areas. Dietary intake of nutrients and serum concentrations of these minerals, however, were not determined in the inhabitants of this area.

Objectives: To examine risk factors for developing ALS in the focus area, with special reference to food intake and essential minerals.

Methods: Blood samples were collected from inhabitants over the age of 40 in the K area (n = 430), the control area (n = 273) and from ALS patients in the Kii Peninsula (n = 95). Serum concentrations of Ca, Mg, Copper (Cu), Zinc (Zn), intact-parathyroid hormone (PTH) and insulin-like growth factor (IGF)-I were determined. A self-administered food frequency questionnaire (FFQ) was used to survey participants who agreed to answer the questionnaire. The differences in mean values or frequencies were statistically examined by unpaired t-test, chi-square test, or Mantel-extension test. The odds ratios (ORs) were estimated using multiple logistic regression models to access the strength of association between ALS and potential risk factors.

Results: A higher proportion of carbohydrate intake and a lower proportion of fat intake was found in ALS patients and in the inhabitants of K area compared to the controls ($P < 0.05$). Dietary intake of Ca was lower in ALS patients than in controls. The ALS patients showed significantly lower concentrations of serum Ca, Cu, Zn and albumin ($P < 0.0001$, respectively) and a tendency toward lower concentrations of intact-PTH compared to those of controls. The inhabitants of K area showed lower serum concentrations of Ca ($P < 0.001$), Cu ($P < 0.02$) and intact-PTH (not significant) and higher concentrations of Zn ($P < 0.05$) than those of controls. There was an inverse relationship between serum concentrations of Ca (lowest vs. highest tertile OR: 0.31 for K area; 0.15 for ALS), Cu (0.92 for K area; 0.12 for ALS) and intact-PTH (0.90 for K area; 0.18 for ALS) and the risk of ALS.

Discussion and Conclusions: It has previously been reported that a high intake of carbohydrate and a low intake of fat increases the risk of ALS. The inhabitants of K area showed similar trends toward dietary intake of nutrients and serum concentrations of essential minerals to ALS patients in the Kii peninsula. These findings suggest that a high proportion of carbohydrate intake with low proportion of fat intake and low serum concentrations of Ca, Cu and intact-PTH might be associated with an increased risk of ALS on the focus area in the Kii Peninsula.

P148 DIETARY PATTERNS AND RISK OF AMYOTROPHIC LATERAL SCLEROSIS IN JAPAN

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Keywords: dietary pattern, meat, epidemiology

Background: Few human studies have reported the relationship between dietary factors and the risk of developing amyotrophic lateral sclerosis (ALS).

Objectives: To examine the relationship between dietary and the risk of developing ALS using a case-control study in Japan.

Methods: The study comprised of 183 ALS patients diagnosed by El Escorial World Federation of Neurology criteria and 407 gender- and age- matched controls that were randomly selected from the general population. A self-administered food frequency questionnaire was used to estimate pre illness intake of food groups and nutrients.

Results: Principal components factor analysis with promax rotation was used to identify 4 patterns that accounted for 38% of the variance of dietary intake frequency: a vegetable-rich pattern, protein-rich pattern (soy products and fish), western-type diet pattern (bread, eggs, red meat and butter) and traditional diet pattern (rice, miso-soup and salted product). Compared to the lowest tertile of the traditional diet pattern, the highest tertile was positively associated with the development of ALS (OR = 2.68; 95% CI: 1.68–4.27; P = 0.001) after adjustment for confounders. The multivariate-adjusted OR for the highest, compared with the lowest tertile of western diet pattern was 0.59 (95% CI: 0.37–0.94; P = 0.02), for the vegetable-rich pattern was 0.64 (95% CI: 0.40–0.95; P = 0.02) and for the protein-rich pattern was 0.48 (95% CI: 0.30–0.75; P = 0.001). Although OR for subjects with only a traditional diet pattern was not significant, that of subjects with traditional diet pattern and one or more dietary patterns among three patterns (vegetable-rich, protein-rich and western-type

diet pattern) were statistically significant (OR: 1.05 for only traditional diet pattern; p for trend = 0.94; OR:5.74 for traditional diet pattern and all three dietary patterns, P = 0.002).

Conclusions: This is the first epidemiological finding that suggests that a dietary pattern with a high intake of carbohydrates such white rice may increase the risk of developing ALS and diets of high-fat and protein foods from animal and vegetable sources may be protective against the onset of ALS.

P149 LIPID PROFILES IN PATIENTS WITH ALS AND ALS MOUSE MODEL

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Keywords: lipid, metabolism, sexual difference

Background: Amyotrophic lateral sclerosis (ALS) is a progressive degenerative disease of motor and extra-motor systems and its exact mechanism and risk factors are still unclear. Recently, abnormally increased lipid metabolism was found in an animal model of ALS and dyslipidemia was reported to be a prognostic factor in patients with ALS.

Objectives: To investigate the lipid profiles of patients with ALS and mouse models of ALS.

Methods: A review of clinical records and serum lipid profiles and fasting glucose of patients with ALS (n = 95, 60 males, mean age: 54.14 years, mean disease duration: 13.44 months) was performed. Patients with significant dysphagia, duration of disease more than 3 years, or PEG (percutaneous endoscopic gastrostomy) were excluded. Control patients consisted of age-sex matched healthy people (n = 99, 62 males, mean age: 52.52 years). Basal serum lipid profiles and fasting glucose, daily dietary intake and weight were also evaluated in the ALS mouse model.

Results: Basal serum level of cholesterol, triglyceride, LDL/HDL ratio and protein was significantly decreased in patients with ALS (n = 95), compared to controls (n = 99, P < 0.005). This decreased serum level of lipoprotein was only observed in male patients and not in female patients with ALS. As for the ALS mouse model, at early symptomatic stage (90 days of age after birth), nine G93A mutated transgenic mice showed significantly decreased serum level of LDL (11.60 mg/dL in G93A versus 16.44 mg/dL in wild type, P = 0.035) and LDL/HDL ratio (0.20 in G93A versus 0.25 in wild type, P = 0.028), compared to ten control wild type mice. The mean amount of dietary intake (3.95 g/day in G93A versus 3.8 g/day in wild type, P = 0.235) and mean body weight (22.73 g in G93A versus 23.69 g in wild type, P = 0.496) did not differ significantly between these groups.

Conclusions: Patients with ALS and a mouse model of ALS both have a decreased serum level of lipid as compared to controls. However, this is not explained by decreased nutritional intake because the mouse model had intact nutritional intake compared to controls. Further to this, the patients with ALS had a lack of significant dysphagia. Further studies about the central nervous system lipid metabolism in ALS mouse models are in progress.

P150 LEVELS OF CHOLESTEROL AND ALS SURVIVAL: A RETROSPECTIVE SURVEY OF 103 PATIENTS

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Keywords: cholesterol, survival, prognosis

Background: ALS is a degenerative disease of unknown etiology. The presence of high levels of cholesterol and triglycerides has been described in several works, as well as their association with survival.

Objectives: To study the relation between the level of cholesterol and the survival of a group of ALS patients.

Methods: A retrospective survey of 103 deceased patients with an ALS diagnosis, defined according to El Escorial criteria was conducted. The levels of cholesterol were measured through blood analysis, after the onset of the disease and without considering the evolutionary moment. Other factors, which have already been associated with ALS survival, have also been valued: delay of diagnosis, site of onset, age of onset, treatment with Rilutek. Furthermore, other criteria have been introduced to determine the nutritional state at the time of the blood analysis.

Results: Among the 103 patients, 63 of them had a high level of cholesterol. No relation has been found between the level of cholesterol and survival through the statistical analysis. However, the correlation between age, site of onset and delay of diagnosis was significant, as it is already known. In this group of patients, no relation has been observed between treatment with Rilutek and survival.

Discussion: There are discrepancies in the different published works about the correlation between cholesterol and ALS survival. Some authors postulate the presence of metabolic alterations, associating hypercholesterolemia with an increase of survival and questioning the use of statins in those patients. The potential link is unknown.

Conclusions: In the group of patients studied, the statistics do not demonstrate a significant relation between cholesterol and survival. This corroborates the already known relation of factors such as the site and age of onset and the delay of diagnosis. It would be necessary to conduct prospective surveys with serial cholesterol evaluations, nutritional state and lipid metabolism data's evaluations, to confirm or infirm the hypothesis of this relation.

P151 DIFFERENT EFFECT OF STATINS ON THE FUNCTIONAL DECLINE OF MEN AND WOMEN WITH AMYOTROPHIC LATERAL SCLEROSIS

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Keywords: statins, gender influence, functional decline

Background: Treatment with statins has been suggested to possibly increase the incidence of amyotrophic lateral sclerosis (ALS), although a recent analysis by the US Food and Drug Administration (FDA) of data from 41 clinical trials did not show a link between statins and a higher risk of ALS and a

retrospective study did not find a negative effect of statins on survival of ALS patients.

Objectives: To further evaluate whether the use of statins for dyslipidemia has an effect on the rate of functional decline in ALS patients.

Methods: This is a retrospective cohort study based on databases created from files of 594 ALS patients who were assessed for a year. The databases were originally created during two clinical trials by the Northeast ALS consortium which evaluated the efficacy of topiramate and celebrex in ALS patients. The protocols and results of both studies have been published. Since both drugs had no effect on ALS progression compared to placebo, all patients were regarded as placebo treated. For all patients the intake of statins at onset and during the study was known. The functional decline was measured by the ALS Functional Rating Scale (ALSFRS) in the topiramate study and the revised scale (ALSFRS-R) in the celebrex study. The follow-up was performed every two months in the celebrex study and every three months in the topiramate study. The functional decline was compared in each study in patients taking or not taking statins over the follow-up period of one year.

Results: The topiramate trial included 294 patients (189 men, 64.3%), with 26 patients (8.8%) on statins, among them 19 men. The celebrex trial included 300 patients (194 men, 64.7%), 22 (7.3%) of them on statins, among them 15 men. Baseline ALSFRS/-R were similar in statin treated and not treated patients in both trials. As expected, the statin treated patients were older in both studies. The ALSFRS/-R declined significantly with time. There was no significant difference between the functional decline with time of all patients taking statins as compared to that of those not taking statins in each study after adjustment for age. However, the functional decline of women taking statins was significantly greater compared to men taking statins in both studies ($P = 0.005$ in the topiramate trial, $P = 0.028$ in the celebrex trial).

Conclusion: This study indicates that women, in contrast to men, are negatively affected by statin treatment. As women are less affected by ALS and are less represented in clinical trials, analyses that do not take into account gender differences might miss important information.

P152 THE USE OF MORTALITY DATA AS SURROGATE OF INCIDENCE IN AMYOTROPHIC LATERAL SCLEROSIS

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Keywords: mortality, incidence, death certificates

Background: Assessing incidence rates for Amyotrophic Lateral Sclerosis (ALS) through morbidity studies is unusual due to uncertain feasibility and high costs. Mortality data have frequently been used to estimate incidence but the accuracy of such a perspective has to be questioned.

Objectives: To identify, through a systematic review, the methodological prerequisite allowing the use of mortality rates of ALS as a surrogate of incidence rates. A Medline literature search was performed to identify (until 2009), studies on ALS and motor neuron disease (MND) mortality rates. The mesh-terms were "ALS", "MND", "mortality", "incidence". Additional references were identified from article citations.

Discussion and Conclusions: Five methodological points have been proposed to be critically assessed when considering a mortality-data-based study. 1) Mortality data must be based on underlying and contributory causes of death. 2) A study (that could be nested in mortality study) about the quality and accuracy of death certificates should be performed or available for the country and period of time that is investigated (true positivity rate, positive predictive value, proportion of unknown causes overall). 3) To compare mortality data among calendar times, using a uniform international classification of diseases (ICD) is essential (ICD 6–8 and 10 on one hand and 9 on the other hand). 4) To compare mortality data among regions, comparable health care systems and death certificate systems (in term of high quality) are essential. 5) To compare mortality data between ethnic groups, critical approach of data (ethnic, access to health care) is indispensable.

P153 THE ACCURACY OF DEATH CERTIFICATION FOR ALS/MND IN IRELAND

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Keywords: death certification, epidemiology, register

Background: Death certification is a recognized means of ascertaining Motor Neurone Disease (MND), although this method has been shown to be less complete when compared to prospective population-based incidence studies.

Objectives: To determine the sensitivity and specificity of death certification for ALS/MND in the Republic of Ireland. The Irish MND Register, which has been in operation for 15 years and seeks to identify all incident patients with MND in the Republic of Ireland using multiple sources of ascertainment, was used to identify all known patients who died from MND from 2002-2006. The Irish Motor Neuron Disease Association was used as a separate verifiable source. The Central Statistics Office (CSO) provided death certificates of individuals over 15 years of age for whom MND (ICD9) was listed as a primary, secondary or tertiary cause of death during the same period.
Cases common or specific to each source were determined to establish the sensitivity and specificity of the death certification process for MND in Ireland.

Results: The cause of death was correctly identified by the CSO as MND in 299 out of 394 (76%) cases known to the Register during the study period. Ninety five (24%) cases known to have died from MND in Ireland were not classified as such on death certification.
Conversely, during the study period, MND was listed as a cause of death by the CSO in 71 cases that were unknown to both the MND Register and the IMNDA database. This represented 20% of all those listed by the CSO. In the majority of these, MND was listed as a secondary/tertiary cause of death and the place of death was more likely to be a rural hospital or nursing home, where diagnostic accuracy is often limited. The absence of demographic detail limited further efforts to verify the diagnosis.

Conclusions: Death certification for MND in Ireland lacks sensitivity and specificity, although the accuracy is similar to that reported in other countries. Prospective identification of

patients using the Irish Register for ALS/MND remains the most accurate method for case ascertainment.

P154 CROSS-SECTIONAL STUDY ON TREATMENT OF AMYOTROPHIC LATERAL SCLEROSIS IN CHINA

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Keywords: multidisciplinary care, cross-sectional study, treatment

Background: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder. A few treatments are now available including riluzole, respiratory care and nutritional support. Multidisciplinary ALS care can produce important benefits in survival, function and quality of life for patients with ALS. The current situation of the treatment for ALS will be revealed in this study.

Objectives: To find out the treatment situation of ALS in China.

Methods: Data on patients with ALS were collected from 9 ALS or neuromuscular disease centre in different geographical regions in China from 1 February 2009 to 30 April 2009. The treatment history was investigated including treatment with medicines, respiratory care, nutritional support and other multidisciplinary care.

Results: Two hundred and forty patients with ALS were included. They consisted of 152 men and 88 women. One hundred and six patients had clinical definite ALS, 61 with clinical probable ALS and clinical probable ALS-laboratory supported, 44 with clinical possible ALS, 29 with progressive muscular atrophy. At the time of investigation, the mean age was 53.9 ± 12.4 years, ranging from 21 to 88 years; the P_{50} of duration from first symptom to investigation was 12.1 months, ranging from 3 to 84 months. Seventy three patients (30.4%) were treated with Riluzole, P_{50} of the duration of treatment with Riluzole was 2 months (from 0.1 to 21 months); 46 patients (19.2%) stayed on Riluzole since the diagnosis whilst the major reason for Riluzole being discontinued was cost (25.9% of patients). Adverse effects were found in 20% of patients and no effect was found in 31%. Thirty patients (12.5%) received psychological treatment, 10 patients (4.2%) were given antidepressants. Twenty seven patients (11.3%) received physical therapy. Five patients accepted stem cell treatment in two different hospitals. Seventy eight patients (32.5%) would like to accept percutaneous endoscopic gastrostomy (PEG) and 66 patients (27.5%) would like to accept nasal feed. Ninety nine patients would like to accept bimodal positive airway pressure (BIPAP) assistance, of whom 44 patients would like to accept tracheotomy when it is necessary.

Discussion and Conclusions: The treatment with Riluzole in patients with ALS in China is much less than those in developed countries because of economic reasons and no obvious effect. Multidisciplinary care should be emphasized to improve the quality of life for patients with ALS. The percentage of patients who would like to accept tracheotomy and invasive mechanical ventilation is more than those reports from developed counties.

P155 PROSPECTIVE GENETIC AND ENVIRONMENTAL EPIDEMIOLOGICAL STUDY OF ALS

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Keywords: family studies, genetics, environmental epidemiology

Background: Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease of unknown etiology. Research suggests ALS is multifactorial in origin, including genetic, environmental and lifestyle factors. Agricultural chemicals, heavy metals, vigorous physical activity, smoking, high glutamate and fat diets have been positively associated with ALS. Prevalence of Parkinson's disease (PD) and Alzheimer's disease (AD) have been reported as higher in ALS patient families than in non-ALS families while other studies report no association. Positive associations of ALS with neurological disease in families may indicate a common genetic or familial origin.

Objectives: To examine genetic, environmental and lifestyle factors associated with ALS and then identify gene-environment interactions.

Methods: ALS patients were enrolled sequentially from an ALS clinic. Patients' siblings, married-in control and married-in control siblings were enrolled. Friend controls enrolled when married-in controls were unavailable. This design provides an opportunity to examine several facets of genetic factors found in ALS patients versus non-ALS subjects. Subjects had blood drawn for cell line or DNA extraction and completed structured interviews on disease history in first degree relatives and environmental exposures. Prevalences of ALS, PD, AD (including related dementias) and Essential Tremor (ET) were measured in all subjects.

Results: From 2005-2009, 101 ALS patients, 72 siblings, 44 married-in controls, 22 siblings of married-in controls and 20 friend controls enrolled. The number of enrolled sibling and control subjects was lower than anticipated. Recruitment of siblings and controls was difficult for several reasons. Either they did not exist, were not contacted by patients, or enrolled but were lost to follow up before data collection. For the family history of neurological disease analysis, information was found on 388 first degree relatives of ALS patients and 266 first degree relatives of controls (married-in and friend controls). Using chi-square methods, no difference was found in the relative risk of ALS, PD and ET relatives of ALS patients versus of other types of unrelated controls. Higher risk of AD was found in friend control relatives versus ALS patient relatives (relative risk $= 0.62$, $P = 0.007$). When data was evaluated on a family level rather than an individual level, there was no significant difference in disease risk between the cases and unmarried controls. Mean ages of the three groups were not significantly different.

Discussion: These results suggest little or no genetic link between ALS and either PD, AD or ET. Type II error is possible given the low number of unmarried controls and low prevalence of these neurological diseases. In addition, the high prevalence of AD in friend controls may indicate some selection bias.

Conclusion: This study design can provide interesting data on genetic and environmental factors associated with ALS. These results also demonstrate the need to consider and minimize control selection bias.