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Regional North American Annual Meeting of the World Federation of Neurology – Research Group on Neuroepidemiology

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Program and Abstracts

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Program

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Oral Presentations

O1

Long-Term Survival of Amyotrophic Lateral Sclerosis: A Population-Based Study

E. Beghi, A. Millul, P. Messina, E. Pupillo, P. Rosettani

Milano, Italy

Objective: To calculate the 10-year survival rate of amyotrophic lateral sclerosis (ALS) in a population-based cohort of newly diagnosed patients. **Background:** There are few published reports on the long-term survival of ALS in representative samples of the general population. **Methods:** All consecutive patients recruited in a population-based registry during the calendar year 1999 in nine provinces of Lombardy, Northern Italy (population 4,947,554) were followed until death or to October 31 2010, whichever came first. For each patient the following prognostic predictors were registered: age, sex, date of onset of symptoms, site of onset (bulbar/generalized vs. spinal), date of diagnosis, El-Escorial diagnostic category. Survival was assessed using Kaplan-Meier curves. Comparisons were made with the log-rank test. The Cox's proportional hazards function was used for multivariable analysis of data to identify independent prognostic predictors. **Results:** The sample comprised 96 patients (46 women and 50 men aged 18 to 88 years). Vital status was not available for 8 cases. Spinal-onset ALS was present in 65 cases (67.7%). Disease duration at diagnosis ranged from 0 to 39 months. Definite ALS was diagnosed in 43 cases (44.8%), probable ALS in 29 (30.2%), possible ALS in 21 (21.9%), and suspected ALS in 3 (3.1%). The cumulative time-dependent probability of survival at 1, 5, and 10 years was 82.0, 26.4, and 11.5%. Independent predictors of 10-year survival were age (HR=1.036, 95% CI: 1.014–1.059) ($p=0.0014$) and disease duration at diagnosis (HR=0.945, 95% CI: 0.911–0.980) ($p=0.0022$). **Conclusions:** The outcome of ALS varies across patients. Longer survival is predicted by younger age and longer disease duration at diagnosis.

O2

Mortality Due to Multiple Sclerosis (MS) in Canada from 1995 to 2004

S. Warren, K.G. Warren, L.W. Svenson, K.V.L. Turpin

Edmonton, Alta., Canada

Objective: The purpose of this study was to describe mortality due to MS in Canada from 1995 to 2004, including peak age at death. **Background:** Previous research indicates that the crude average annual MS mortality rate in Canada during 1990–94 was 0.96 per 100,000 population. Mortality peaked in individuals aged 60–69; 76.20% of patients died before age 70. **Methods:** Information on deaths due to MS (2000–04 being the last 5-year period available) and populations at risk was derived from Statistics Canada

public domain databases. Statistics Canada codes MS as a primary or underlying cause of death, using the most current version of the International Classification of Diseases. **Results:** Crude average annual MS mortality rates per 100,000 population during the 5-year periods 1995–99 and 2000–04 were 1.13 and 1.34 respectively. Age-specific mortality rates confirmed the increase was not due to a difference in age distribution between periods. Mortality rates increased with age during each 5-year period, peaking in individuals aged 80+ in both 1995–99 and 2000–04; 69.14% and 69.74% of patients died before age 70 respectively. The age-specific mortality rate profile for 1995–99 was 0.13 for <40 years of age, 1.27 for 40–49, 2.20 for 50–59, 3.47 for 60–69, 4.24 for 70–79 and 4.52 for 80+. The 2000–04 profile was 0.12 for <40 years, 1.54 for 40–49, 2.55 for 50–59, 3.77 for 60–69, 4.57 for 70–79 and 4.95 for 80+. Crude average annual mortality rates were higher in women than men, with ratios of 1.68 for both 5-year periods. **Conclusions:** Mortality due to MS is increasing modestly in Canada, with peak age at death apparently shifting to later years. This shift may indicate that life expectancy is increasing among MS patients due to better health care or may be related to diagnosis of milder cases following introduction of techniques like MRI.

O3

Genotype and Age at Parkinson Disease Diagnosis in Health Maintenance Organization

S. Searles Nielsen, L. Gallagher, J. Lundin, W.T. Longstreth Jr., F. Farin, T. Smith-Weller, G. Franklin, P. Swanson, H. Checkoway

Seattle, Wash., USA

Objective: To investigate whether single nucleotide polymorphisms (SNPs) in candidate genes (e.g. oxidative stress and inflammation) are associated with age of diagnosis of idiopathic Parkinson disease (PD). **Background:** Genotypic influences on age at PD onset or diagnosis have been examined frequently. Often, however, cases' health care coverage varies, and there is no verification that genotype is independent of longevity among non-cases. **Methods:** We characterized >3000 SNPs for 758 non-Hispanic Caucasians: 257 newly diagnosed cases (39–88 years old, mean 67) enrolled at Group Health Cooperative (GHC) in western Washington, 64 cases from the University of Washington (UW), and 437 sex- age-matched, neurologically-normal, unrelated GHC controls. Because smoking is associated with PD, longevity and genotype, we used never-smoking GHC cases ($N=126$) and controls ($N=170$) to identify SNPs associated with diagnosis age, but not similarly associated with attained age among controls. We further restricted comparisons to SNPs showing a similar association among never-smoking UW cases ($N=36$), and which have potential for functional effects. **Results:** Only rs10889162 met all criteria. This SNP is near the *PARK10* region in a transcription factor binding site 5' of *CYP2J2*. *CYP2J2* epoxigenase is anti-inflammatory, anti-apoptotic and prevalent in the substantia nigra. Non-smoking GHC cases with one variant allele were diagnosed 5.8 (95% confidence interval [CI] 1.4–10.2) years later than homozygous wildtype cases (homozygous variants unobserved). Similar associations were seen among never-smoking UW cases (3.9 years, $p=0.44$), ever-smoking GHC cases (4.0 years, $p=0.06$)

and ever-smoking UW cases (8.9 years, $p=0.06$). A combined ($N=321$) estimate (5.1, 95% CI 2.3–7.8 years) was unattenuated by exclusion of cases with a first degree relative with PD. This association was absent among controls (-0.3 years, $p=0.81$). **Conclusions:** These biologically plausible results parallel those reported in other Caucasian samples for loci in or near the *PARK10* region. However, the relevance of *CYP2J2* specifically requires confirmation.

O4

Dementia Risk in Parkinson's Disease: The Honolulu-Asia Aging Study

K. Tomita, Q. He, W. Ross, H. Petrovitch, K. Masaki, C. Tanner, L. White

Honolulu, Hawaii, and Sunnyvale, Calif., USA

Objective: To examine the risk of dementia among elderly Japanese-American men with Parkinson's disease (PD) compared to age matched controls in the Honolulu-Asia Aging Study. **Background:** Previous studies have shown that risk of dementia in persons with PD is 4 to 6 times that in similarly aged controls. Few factors other than age have been identified as influencing the development of dementia in PD. **Methods:** Data are from the longitudinal, population based HAAS, a continuation of the Honolulu Heart Program. PD cases were identified at cohort examinations performed in 1991, 1994, and 1997, and were free of dementia at the time follow-up began. Four controls without PD or dementia were selected for each PD case, matched for age and exam at which the corresponding PD case was first identified. Dementia was identified using standardized procedures and research diagnostic criteria during cohort examinations in 1994, 1997, and 1999. Follow-up for dementia occurred for up to ten years. Cox proportional hazards modeling was used to compare risk for developing dementia in PD cases vs controls. **Results:** Dementia developed in 22 of 103 PD cases compared to 22 of 412 controls over the period of follow-up. The hazard ratio for dementia for PD vs. controls was 6.5 (95% confidence interval: 3.6, 11.9). **Conclusions:** Risk of dementia among older Japanese American men with PD living in Hawaii is high and approximates that of previous reports from other longitudinal studies.

O5

Stimulant Use and Risk of Parkinson's Disease

S.K. Van Den Eeden, K.B. Albers, C.M. Tanner, L.M. Nelson

Oakland, Sunnyvale, and Stanford, Calif., USA

Objective: To examine the risk of Parkinson's disease (PD) associated with stimulant use. **Background:** Two studies have reported that amphetamines use was associated with an increased risk of Parkinson's disease. **Design/Methods:** Our study population was the participants in the Parkinsonism Epidemiology in

Kaiser 3 (PEAK3) case-control study. Cases were individuals under the age of 60 years who were newly diagnosed individuals with idiopathic Parkinson's disease while a member of Kaiser Permanente Northern California between 2000 and 2005. Cases ($n=174$) were determined by confirmed by expert review of KPNC electronic clinical records. Controls ($n=191$) were matched to cases based on age and sex. Exposure to amphetamines was determined by questionnaire regarding the use of legal and illegal drugs, including stimulants. Logistic regression was used to estimate the odds ratio (OR) and 95% confidence intervals (CI) associated with stimulant use, after adjusting for confounders. **Results:** Mean age on onset for cases was 53.3 years. Cases were, on average, less likely to smoke, and drink more coffee compared to controls. Cases and controls had similar body mass index distribution. Nine cases and five controls reported stimulant use. The OR for use of stimulants was 2.01 (0.63–6.45). **Conclusions:** While the association between stimulants and an increased risk of Parkinson's disease was similar to recent studies, we cannot rule out chance in this study.

Poster Presentations

P1

Clinic-Based Protocol for Enhancing Patient Entry into CDC National ALS Registry

B. Rix Brooks, E. Bravver, N. Williams

Charlotte, N.C., USA

Objective: To enhance patient entry into CDC National ALS Registry. **Background:** The Center for Disease Control (CDC) National ALS Registry was launched in October 2010. The Carolinas Neuromuscular/ALS-MDA Center at the Carolinas Medical Center established a protocol of placing contact information for the CDC ALS Registry together with a CDC ALS Registry decal on discharge instruction forms for each patient at monthly ALS multidisciplinary clinics. **Methods:** At the subsequent quarterly follow-up clinics, ALS patient registration in the CDC National ALS Registry was ascertained. Non-registrants received an additional review of the ALS Registry goals with the CDC ALS Registry brochure, a description of possible future studies to be conducted by the CDC ALS Registry and an additional telephone call one week later. **Results:** After the first announcement of the CDC ALS Registry, 39 of 67 (58.2%) patients registered in three clinic cycles. Following the review of the CDC brochure with the initial (41.8%) non-registrants, an additional 11/28 (39.3%) secondary registrants (16.4%) contacted the CDC ALS Registry. The remaining 17 non-registrants (25.4%) were further along in mean disease duration from onset [42 months vs 33 months] and had lower ALSFRS-R [25 vs 36] than ALS Registry registrants. Age, sex, site of ALS onset, or riluzole treatment were not discriminating factors. **Conclusions:** An established protocol to present the CDC National ALS Registry to a clinic population of ALS patients

achieved registration status in 74.6% of ALS patients in two iterative cycles. Further cycles are being implemented to try to increase the proportion of ALS patients registered in the CDC National ALS Registry.

P2

Burden on Caregivers of Stroke Survivors: Prospective Population-Based Study in Mumbai (India)

M. Bhattacharjee, J. Vairale, K. Gawali, P.M. Dalal

Mumbai, Maharashtra, India

Objective: To identify factors related to increased care giver burden in stroke survivors in a well defined population in Mumbai, and to assess the relationship between patient characteristics and caregiver stress. **Background:** India is facing socioeconomic burden to meet the costs of integrated rehabilitation of stroke patients. Caring for stroke subjects leads to caregiver (CG) strain, but focus on CG stress is a neglected domain. **Methods:** During prospective study period (Dec 2008–Nov 2009), 223 first ever stroke (FES) subjects were identified. At 28 days, 127 (56.9%) were alive 79 (35%) died, and 17 were lost to follow-up. 111 Caregivers of 127 FES survivors, agreed to participate. The level of stress was assessed by Oberst Caregiving Burden Scale (OCBS) and the Caregivers Strain Index (CSI) in CGs of survivors with mild stroke Modified Rankin Scale (MRS 1–2) and in those with significant disability (MRS 3–5). **Results:** The mean age of CGs was 45.6 years. 89 (80%) of CGs were females and only 22 (19.8%) were males. Urinary incontinence ($p=0.000008$), morbidity at 28 days by Modified Rankin Scale ($p=0.0051$), female gender ($p=0.0183$), moderate to severe neurological deficit by National Institute of Health Stroke Scale (NIHSS) on admission ($p=0.0254$), were factors in FES cases leading to major CGs stress. CG factors responsible for major stress were long caregiving hours ($p<0.000001$), anxiety ($p<0.000001$), disturbed night sleep ($p<0.000001$), financial stress ($p=0.0000108$), younger age ($p=0.0021$), and CGs being daughter-in-laws ($p=0.012$). However, CGs education, occupational status and marital status were not significantly related to CG stress. **Conclusion:** There are no organized stroke care delivery systems for the patient neither any support system for the CG in India. Integrated stroke rehabilitation services should address caregiver issues to local situations. Practical training in simple nursing skills and counseling sessions will help reduce CG burden.

P3

Bending the Opioid Dosing Curve: Impact of the WA State Opioid Dosing Guideline

G. Franklin, J. Mai, T. Wickizer, J. Turner, M. Sullivan, D. Fulton-Kehoe

Olympia, Wash., Columbus, Ohio, USA

Objective: To determine if a statewide opioid dosing guideline implemented in April 2007 has impacted opioid dosing and mortality in the WA workers compensation (WC) system. **Background:** Since the late 1990s, more permissive laws and other factors have led to a dramatic rise in use of high doses of potent (Schedule II) opioids for chronic non-cancer pain in the US. This has led to an epidemic of unintentional poisoning overdose, now the leading cause of injury death in the 35–54 year age group. To address this public health crisis, Washington State implemented an opioid dosing guideline for prescribing practitioners in April, 2007. The guideline established a ‘yellow flag’ 120 mg/day morphine equivalent dose (MED) as a warning threshold for evolving opioid tolerance. **Methods:** Detailed computerized paid pharmacy bills were used to determine patterns of opioid dosing between 1999–2009. The MED/day for all long-acting Schedule II opioids was calculated by quarter. Mortality was determined using death record review and a previously published case definition of definite, probable, and possible death related to unintentional overdose from prescribed opioids. **Results:** As we previously reported for the WA workers’ compensation system, average MED/day rose from 80 mg/day MED in 1999 to over 140 mg/day by 2002, then stabilized. At the same time, increasing mortality occurred. Since the introduction of the WA guideline in 2007, average MED dropped to under 110 mg/day by 2009; mortality in WC, however, has not yet declined. Statewide mortality and overdose hospitalization data has, however, shown moderation. **Conclusions:** For the first time in more than a decade, opioid dosing patterns in the WA workers’ compensation system have declined for the most potent, long acting Schedule II opioids, likely due to the WA state opioid dosing guideline and other efforts. Mortality in WC, however, has not yet declined, likely due to persistence of some patients on more extreme doses combined with other comorbidities.

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