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Program and Abstracts

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Program

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Oral Presentations

O1

First Population-Based Survey of Epilepsy in Gabon, Central Africa

E.B. Ngoungou, F. Quet, G. Mouangue Minso, Y. Assengone-Zeh, D. Houinato, M. Druet-Cabanac, M.A. Saphou Damon, P. Kouna-Ndouongo, D.C. Akerey Diop, P.-M. Preux

Limoges, France and Libreville, Gabon, and Cotonou, Bénin, Africa

Objective: To estimate the prevalence of epilepsy in a semi-rural area of Gabon (first population-based survey in this country). **Background:** Prevalence of epilepsy in Africa is high (median prevalence: 15% - Preux & Druet-Cabanac, 2005). However, no data exist in several countries, as in Gabon although 7 neurologists are working there. Data are important to sensitize health authorities and allocate specific resources. **Methods:** Door-to-door survey was done in 2005 in the area of Ntoun, 40 kms west from the capital Libreville. First a screening phase was implemented using the Limoges Questionnaire for Investigation of Epilepsy in Tropical Countries (Preux et al., 2000). This questionnaire has been validated in Mauritania (Diagana et al., 2006) leading to a sensitivity of 95% (CI95%: 87–98). Two other sources of information were used: non-medical source (traditional healers, head of the villages, teachers, religious leaders) and medical source (medical registries, pharmacies...). A neurologist examined all suspected cases identified in any of the sources and confirmed or not epilepsy. Epilepsy was defined using epidemiological definition of those of ILAE, 1993. Capture-recapture method was used to estimate the number of people with epilepsy missed by all sources. **Results:** Out of 6259 included subjects, 48 people with epilepsy were identified by door-to-door survey leading to a prevalence of 7.7% (CI95% 5.7–10.2). Furthermore, 16 people with epilepsy were confirmed by non medical source and 8 by medical source. In total, 51 cases were confirmed by the 3 sources. Capture-recapture methods estimated 58 cases in total, then a prevalence of 9.3% (CI95% 6.9–11.7). Only 13.8% of the cases were treated for their epilepsy. **Conclusions:** Prevalence was slightly lower than expected. Use of several sources of information could be useful as already found in Benin (Debrock et al., 2000). The treatment gap is huge. Actions will be implemented in Gabon.

O2

Hospitalizations for Infections and Surgery Trigger Acute Ischemic Stroke

C. Carty, E. O'Meara, T. Lumley, D. Lefkowitz, R. Kronmal, W. T. Longstreth, Jr., M. Elkind

Seattle, Wash., USA

Objective: To determine whether hospitalization for infection or surgery triggers acute ischemic stroke. **Background:** Triggers of

acute ischemic stroke are largely unknown. Do strokes occur randomly or do factors such as infection or surgery trigger them? We investigated associations between hospitalization for infection or surgery and risk of acute ischemic stroke in the prospective Cardiovascular Health Study, a biracial cohort of 5888 elderly participants from four US sites. **Methods:** Using a case-crossover design in which participants served as their own controls, we analyzed data from 667 participants without history of stroke at baseline but who had incident ischemic stroke during a median 12.2 years of follow-up. Exposure was defined as hospitalization for infection or surgery within 90, 30, or 14 days prior to stroke (case period) or during equivalent time periods exactly 1 or 2 years prior to stroke (control periods). Hospitalizations for cardiovascular and neurosurgical procedures were excluded given their known association with stroke. We used conditional logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs). **Results:** Approximately 48% of cases had an eligible hospitalization anytime before their stroke. The OR (95% CI) of stroke following hospitalization for infection or surgery within the previous 90 days was 3.37 (2.22–5.12); 30 days, 6.20 (3.10–12.6); and 14 days, 8.27 (3.14–21.7). ORs for stroke were higher following hospitalization for infection than surgery during all time intervals. **Conclusions:** Hospitalization for infection or surgery is associated with a short-term increase in risk of acute ischemic stroke, with higher risks observed for shorter intervals preceding stroke and for hospitalizations for infection. These findings may be subject to bias from time-varying factors, including age and medication use, although these confounders are unlikely to fully explain associations. Inflammation may explain associations and suggest preventative measures, assuming these associations can be confirmed.

O3

Obesity, Diabetes and Risk of Parkinson Disease in a Large Prospective Cohort of Men and Women

N. Palacios, M. McCullough, E. Jacobs, A. Patel, T. Mayo, M. Schwarzschild, A. Ascherio

Boston, Mass. and Atlanta, Ga., USA

Objective: To investigate if obesity and diabetes are related to risk of Parkinson's Disease (PD). **Background:** Several studies have reported a positive association between obesity, other measures of adiposity and diabetes and risk of PD, while others have been null. **Methods:** We prospectively followed 143,325 participants in the Cancer Prevention Study II Nutrition Cohort from 1992 to 2001. Body mass index (BMI), weight gain since age 18, and history of diabetes were assessed at baseline in 1992 and waist circumference was assessed in 1997. Incident cases of PD ($n = 413$) were confirmed by treating physicians and medical record review. Relative risks (RR) were estimated using proportional hazards models, adjusting for age, gender, smoking and other risk factors. **Results:** Risk of PD was similar across categories of BMI at baseline. The RR comparing individuals with a BMI ≥ 30 to those with a BMI < 23 was 0.96 (95% CI: 0.60, 1.55, p -trend: 0.79) in men and 1.31 (95% CI: 0.76, 2.25, p -trend: 0.26) in women. Neither a diagnosis of diabetes at baseline (RR = 0.61; 95% CI: 0.34, 1.10 in men; and RR = 1.19, 95% CI: 0.60, 2.37 in women) nor waist cir-

cumference (RR comparing the highest to the lowest quintile = 1.08; 95% CI: 0.64, 1.85 in men and RR = 1.12; 95% CI: 0.54, 2.33 in women) were associated with an increased risk of PD. Weight gain between age 18 and baseline was marginally associated with a reduced risk of PD in men but not in women. **Conclusions:** Our results do not support a positive association between BMI, weight change, and baseline diabetes and risk of Parkinson's disease.

O4

Exercise and Survival in Alzheimer's Disease (AD)

N. Scarmeas, S. Cosentino, N. Schup, J. Luchsinger, A. Brickman, Y. Stern

New York, N.Y., USA

Objective: To explore whether physical activity (PA) can prolong survival in AD. **Background:** PA may protect from development of AD and may prolong survival in the general population. Whether it can prolong longevity in patients who have already developed AD has not been explored. **Methods:** Community-based individuals aged ≥ 65 in Manhattan New York were prospectively followed with standard neurological and neuropsychological evaluations (every ~ 1.5 years). PA information was available for 276 participants who were non-demented at baseline were diagnosed with AD during follow-up (incident AD). PA assessments were performed 2.4; sd 1.9 years before incidence and recorded time of participation in light, moderate or severe physical activities. The sum of each subject's overall activities was used as the main predictor of mortality (150 incident AD deaths [54%] during the course of 5.2 [sd 4.4] years of follow-up) in Cox models. Basic models adjusted for cohort, age, gender, ethnicity, education and duration between PE evaluation and dementia incidence, while additional adjustment for APOE, smoking, medical comorbidities, dietary habits, caloric intake and baseline CDR did not change the associations. **Results:** Compared to incident AD cases with no history of PA, those with moderate PA had lower mortality risk (HR: 0.53; 95% CI: 0.34–0.80; $p=0.003$), while those with high PA had an even lower risk (0.41; 0.25–0.67; $p<0.001$) (overall p for trend <0.001). **Conclusions:** AD patients who are more physically active live longer. Therefore, exercise may affect not only risk for AD development but also subsequent disease prognosis. Although reverse causality (PA being an index of AD severity) cannot be excluded, assessing PA before incidence, adjusting for cognitive impairment and considering medical comorbidities, makes this possibility less likely.

O5

Risk of Decline in Functional Activities in Dementia with Lewy Bodies and Alzheimer's Disease

D. Gill, T. Koepsell, W. Kukull

Seattle, Wash., USA

Objective: To determine whether the risk of decline in specific functional activities differs between persons with dementia with Lewy bodies (DLB) and Alzheimer's disease (AD). **Background:** Performance of everyday activities becomes impaired with dementia. These impairments can diminish quality of life for those with dementia and increase burden on both caregivers and the health-care system. Few studies have compared functional decline between DLB and AD. **Methods:** We used data from the National Alzheimer's Coordinating Center, gathered from 31 Alzheimer's Disease Centers. Subjects had a clinical diagnosis of dementia, primary diagnosis of DLB or probable AD, Clinical Dementia Rating scale score between 0.5 and 2.0, age ≥ 55 , and completed a 1-year follow-up visit. The Functional Activities Questionnaire assessed ability to perform 10 activities necessary for independent living. Modified Poisson regression models compared risk of 1-year decline in each activity between DLB and AD, controlling for baseline activity. Age, sex, race, marital status, education, and disease duration were also examined as potential confounders. **Results:** 1813 subjects (DLB=119, AD=1694) were included (76.4 ± 8.4 years; 52% female). DLB subjects were at increased risk of decline on 8 of 10 activities [RR (95% CI): 1.11 (0.85–1.44) to 1.37 (1.12–1.67)]. For two activities (playing games of skill or working on hobbies, going shopping alone), DLB subjects were at significantly increased risk of decline (RR = 1.43, 95% CI=1.16–1.76 for games/hobbies, RR = 1.29, 95% CI=1.06–1.57 for shopping), after adjusting for baseline activity, age, and sex. **Conclusions:** DLB subjects were found to be at increased risk for 1-year decline in several daily activities, especially playing games of skill or working on hobbies and going shopping alone, compared to AD subjects. These results may assist clinicians and families, with planning for a demented individual's need for help with functional activities.

O6

Examination of Paraoxonase Gene Cluster and Vietnam Deployment in Amyotrophic Lateral Sclerosis

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Durham, N.C., USA

Objective: To analyze the association of variants in the paraoxonase (PON) gene cluster and possible exposure opportunity to organophosphates with the risk of ALS in US military veterans. **Background:** Previous studies suggested that variants in the PON gene cluster may be associated with ALS risk. All three PON genes inhibit lipid peroxidation; PON1 is also involved in organophosphate (OP) detoxification. Additionally, studies suggested an increased risk of ALS in US military veterans, for which the cause

is currently unknown. **Methods:** As part of the GENEVA case-control study conducted in conjunction with the National Registry of Veterans with ALS, we have genotyped 1165 ALS patients (98% male, 91% Caucasian) and 530 controls (94% male, 88% white). We tested 12 SNPs in the PON cluster for association with ALS using both single-locus and multilocus methods. We also examined interaction between these genotypes and Vietnam deployment as a crude surrogate for possible OP exposure. **Results:** We did not observe any significant association between PON variants alone and ALS risk. However, for two previously implicated PON1 promoter SNPs, we detected significant differences in the minor allele frequency by Vietnam deployment status in cases (rs705379: 44% vs. 50%, $p=0.024$; rs854571: 28% vs. 35%, $p=0.005$). We did not observe a similar difference for either SNP in controls. This pattern is suggestive of gene-environment interaction, although the product term in a standard logistic regression analysis was not significant. **Conclusions:** Our analysis is consistent with a previous study (Morahan et al. 2007) that examined PON1 genotype frequencies by pesticide exposure status. Although the use of Vietnam deployment status as a surrogate likely involves substantial misclassification of actual OP exposure, these results suggest that a more detailed estimation of the OP exposure opportunity of Vietnam veterans may be warranted.

07

Smoking and Amyotrophic Lateral Sclerosis: A Prospective Study

A. Alonso, G. Logroscino, S. Jick, M. Hernán

Minneapolis, Minn. and Lexington and Boston, Mass., USA and Bari, Italy

Objective: To estimate the association of smoking with (1) the risk of amyotrophic lateral sclerosis (ALS) in the general population, and (2) mortality in patients with ALS. **Background:** Previous studies have shown conflicting results on the association of smoking with incidence of ALS. Limited evidence suggests that the association may be different in men and women. The role of smoking on the prognosis of ALS has been rarely studied. **Methods:** Case-control study nested in the General Practice Research Database (GPRD), a large computerized clinical database in the United Kingdom. ALS cases were identified from the computerized record in the period 1990–2008. Cases were older than 18 years, with at least 2 years of follow-up before the disease diagnosis (index date). Up to 10 controls, free of ALS at the index date, were matched to each case by age, sex, practice and year of enrollment in the GPRD. Information on smoking before the index date was collected from the database. Conditional logistic regression and Cox models were adjusted for potential confounders. **Results:** The study included 1,143 ALS cases and 11,371 controls. In multivariable conditional logistic regression, the rate ratio (95% confidence interval (CI)) of ALS in ever smokers versus never smokers was 1.04 (0.81–1.34) in the entire sample, 0.75 (0.53–1.05) in men, and 1.53 (1.05–2.24) in women (p for interaction=0.01). In ALS patients, smoking was not associated with mortality (hazard ratio (HR) comparing ever versus never smokers: 1.06, 95% CI 0.91–1.24), but results varied by sex: in men, the HR of mortality (95% CI) in ever versus never

smokers was 0.90 (0.72–1.11), while in women it was 1.35 (1.07–1.70) (p for interaction=0.02). **Conclusion:** Smoking was associated with a slightly higher risk of ALS incidence and mortality in women but not in men.

Poster Presentations

P1

Are Motor and Non-Motor Signs in Essential Tremor Due to the Same Pathogenic Process?

E. Louis

New York, N.Y., USA

Objective: The current goal, through factor analyses, was to determine how motor and non-motor signs relate to one another in patients with essential tremor (ET) and furthermore, to shed light on the pathogenic bases of these signs. **Background:** ET has traditionally been viewed as monosymptomatic. However, there is an emerging appreciation of an expanded number of motor manifestations as well as new awareness of non-motor manifestations. **Methods:** One-hundred-thirty-eight ET patients were enrolled in an ongoing cross-sectional, clinical-epidemiological study at the Neurological Institute of New York, Columbia University Medical Center. Each had a detailed neurological examination. **Results:** In factor analyses, three separate factors emerged, explaining 58.7% of the variance. Factor I was comprised of the hallmark feature of ET, action tremor. It also included intention tremor, which is generally viewed as a sign of cerebellar dysfunction, and tremor duration. Factor II was comprised of cognitive test scores and age, and Factor III, of rest tremor. Cognitive test scores did not fall into the same domain as motor features or tremor duration. **Conclusions:** Factor analysis finds relationships or connections between variables that are maximally correlated with one another and minimally correlated with other variables. In the current analyses, the various motor and non-motor manifestations of ET were not comprised of a single dimension, but rather, formed three separable and identifiable clusters. These clusters offer clues about possible underlying pathogenic mechanisms in this poorly-understood yet common disease. These results suggest that: (1) the process that underlies cognitive dysfunction in ET is distinct from that which is responsible for action and intention tremors and their progression over time, and (2) cognitive dysfunction in ET is not likely due to cerebellar degeneration. Age loaded with cognitive test scores, further raising the possibility that age-related processes (e.g., Alzheimer-type changes) could underlie the cognitive changes in ET.

P2**Association between Essential Tremor and Incident Dementia: A Prospective, Population-Based Study in Northern Manhattan***S. Thawani, N. Schupf, E. Louis*

New York, N.Y., USA

Background: Mild cognitive deficits, mainly in frontal-executive function and memory, have been reported in patients with essential tremor (ET). Most recently, an association between ET and incident dementia has been reported in a single population-based study in Spain. This has not been confirmed elsewhere. **Objective:** To determine whether baseline ET is associated with incident dementia in an ethnically-diverse, community-based sample of elders. **Methods:** Community-dwelling elders (age >65 years) in northern Manhattan, New York, were enrolled in a prospective cohort study (the Washington/Hamilton Heights and Inwood Aging Project). Baseline ET diagnoses were assigned from handwriting samples. Non-demented ET cases and controls were followed prospectively. Incident dementia was diagnosed at follow-up using Diagnostic and Statistical Manual of Mental Disorders (III-R) criteria. Cox proportional hazards regression was used to compare the risk of incident dementia in participants with and without ET at baseline. **Results:** There were 2,056 participants (93 ET cases, 1,963 controls). Mean duration of follow-up was 3.8 ± 2.2 years. During follow-up, 17/93 (18.3%) ET cases and 171/1,963 (8.7%) controls developed dementia (unadjusted hazard ratio [HR] = 2.78, 95% CI = 1.69–4.57, $p < 0.001$). Adjustment for age, education, and ethnicity reduced the HR (1.64, 95% CI = 0.99–2.72, $p = 0.055$). When we excluded 316 participants with mild cognitive impairment, the adjusted HR = 2.07, 95% CI = 1.18–3.66, $p = 0.01$ and, after excluding 388 participants with depression, the adjusted HR = 1.76, 95% CI = 1.01–3.07, $p = 0.048$. **Conclusions:** In a second population-based study of elders, ET was associated with increased risk of dementia. Rather than attributing cognitive complaints in ET patients to age-related decline, assessment and possible treatment of dementia should be routinely incorporated into the treatment plan.

P3**Body Size and Category Fluency Decline with Aging: Evidence of Effect Modification by Sex***S. Edland, G. Laughlin, D. von Mühlen, Don. Kritz-Silverstein, J. Bergstrom, D. Salmon, E. Barrett-Connor*

La Jolla, Calif., USA

Background: Recent studies report contradictory results regarding the relationship between body composition measures and age-associated cognitive decline and dementia. We examine this association using longitudinally assessed category fluency scores in a population-based sample of community-dwelling residents of Rancho Bernardo, CA. **Methods:** Participants were 363 women and 285 men aged 50 to 70 years at the time of risk factor assessment (1984–1987) who also had at least two, and up to five,

cognitive assessments of category fluency at approximate three to four year intervals (mean length of cognitive follow-up 11.3 years, range 2.9–17.6 years). Sixty-one percent of participants had four or more cognitive assessments. Mixed effects models were used to test the association of body size and fat distribution measures on category fluency trajectory after stratifying by sex and controlling for age, education (college yes/no), time, time-squared, and interaction terms involving time. **Results:** Women weighed 36.8–110.5 kg (mean 63.4, SD 9.7), and men weighed 58.0–118.5 kg (mean 81.8, SD 10.6). Weight was associated with increased rate of decline within women ($p < 0.05$ for weight by time and weight by time-squared terms). Heavier women declined 0.12 points per year faster per standard deviation increase in weight. A positive weight by time-squared term indicated the effect was attenuated over time. In contrast, weight was associated with decreased rate of decline in men ($p > 0.1$). This same pattern, of a statistically significant negative effect on cognitive trajectory in women and a non-significant effect in the opposite direction in men, was observed for body mass index, waist circumference, and waist:hip ratio (p -values for interaction < 0.05). **Conclusions:** In this community-dwelling cohort, the effect of body composition on category fluency performance was modified by sex, with measures of central and overall adiposity associated with faster decline in women but slower decline in men.

P4**Trends in Dementia and Dementia Subtypes: Findings from an Active Surveillance Program in Electronic Health Records***R. Whitmer, C. Quesenberry*

Oakland, Calif., USA

Objective: 1) To examine how our prevalence and incidence estimates compare with other corresponding population-based estimates of dementia and dementia subtypes; 2) to determine if there are differences in trends by race/ethnic group; 3) to provide population-based estimates of prevalence and incidence among our oldest old patients (age 95+); 4) to give possible explanations for patterns of trends. **Background:** Prior research has shown that dementia is under-diagnosed in the primary care setting and that internists and geriatricians may undercode for dementia and Alzheimer's disease. Some estimates suggest that under-diagnosing for dementia in the primary care setting may range from 10–40%. However, prevalence and incidence rates conducted within an integrated health care delivery plan where participants receive all medical care within one system may not result in as much under-diagnosing as was previously thought and can provide data on longitudinal and secular trends. **Methods:** Using diagnoses of dementia from our primary care setting and diagnoses of dementia subtypes (Alzheimer's disease and vascular dementia) from our Neurology departments and memory clinics, we determined ten year annual and cumulative prevalence and incidence rates in our large diverse population of elderly members of Kaiser Permanente of Northern California aged 60+. For the period January 1, 1998, through December 31, 2007, we examined annual prevalence and incidence rates in the dynamic cohort of

Health Plan members aged 60 or greater. Rates are stratified by seven self-reported race/ethnicity groups (Asian, Black, White, Mixed, Pacific Islander, Native American, and Hispanic). Rates were adjusted using the direct method with the age 60+ United States 2000 Census as the standard population. Annual age-specific incidence and prevalence rates were also examined using the following age groups: 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, and 95+. Age-adjusted prevalence rates increased over the ten year period and varied by race/ethnicity group. **Results:**

Conclusions: Even with the caveats of using electronic medical record diagnoses, data from integrated health care delivery systems can provide useful information regarding longitudinal trends in clinically recognizable dementia among larger, more diverse populations.

P5

Lead Exposure and Amyotrophic Lateral Sclerosis in a Northern California Population

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Oakland and Stanford, Calif., New York, N.Y., USA

Objective: To examine the association between lead exposure and amyotrophic lateral sclerosis (ALS). **Background:** Epidemiologic and laboratory studies have implicated heavy metals, lead in particular, in the etiology of ALS. Previous studies have been inconsistent in their finding of an association between ALS and self-reported non-occupational as well as occupational lead exposure and biological measures of lead. **Methods:** We enrolled 165 incident ALS cases and 389 age- and sex-matched controls in a case-control study of members from the Kaiser Permanente Medical Care Program in Northern California, from January, 1996 thru March, 2000. Blood lead was measured in 113 cases and 319 controls. In addition, 66 cases and 88 controls had patella and tibia lead concentrations measured *via* K-shell X-ray fluorescence, and bone mineral density measured using *via* Dual Energy X-ray Absorptiometry scans. Unconditional logistic regression models were used to compute odds ratios (OR), adjusted for age and sex.

Results: Cases had a slightly higher blood lead level (mean 3.4 $\mu\text{g}/\text{dL}$, SD 2.7) than controls (mean 2.8 $\mu\text{g}/\text{dL}$, SD 2.3). We observed a statistically significant positive association between blood lead levels and ALS. Compared to subjects who had low blood lead levels ($< 3.0 \mu\text{g}/\text{dL}$), those whose blood lead was in the range of 3.0–3.9 $\mu\text{g}/\text{dL}$ had an increased association with ALS (OR=1.8, 95% CI 1.0–3.6); and those with the highest blood lead levels ($\geq 4.0 \mu\text{g}/\text{dL}$) had the highest association with ALS (OR = 2.5, 95% CI 1.4–4.3) (p for trend=0.001). Although some patella and tibia lead concentrations were elevated, there was no association between bone lead level and ALS in this group. **Conclusions:** Although we observed a modest cross-sectional association between blood lead level and ALS, there was no association between bone lead level and ALS.

P6

Rate of Statin Cessations in an ALS Clinic is Significantly Higher Than in a MS Clinic

B. Rix Brooks

Charlotte, N.C., USA

Objective: Identify the rate of initiation and discontinuation of Non-Statins and Statin treatments in an ALS Clinic compared with a MS Clinic. **Background:** Data mining found disproportionate reporting of ALS-like syndromes with Statins in Vigibase, the WHO adverse event (AE) reporting database [Edwards RI, Drug Safe 2007]. The FDA confirmed this increase in the spontaneous AE reporting system [AERS] containing greater than 4 million post-marketing AE reports [Colman E, Pharmacopeidemiol Drug Safe 2008] and reviewed the occurrence of ALS in 41 controlled clinical trials representing 200,000 patient-years finding no difference in new ALS patients and concluded that "... reporting bias should be given serious consideration as a possible explanation for spontaneous reports of ALS ... in patients taking statins." **Methods:** Evaluate Statin discontinuations in patients attending an ALS clinic [$n=240$] or MS Clinic [$n=130$] from 2004–2007. **Results:** Prevalence of diabetes mellitus (DM) [4.6 %, 5.9 %, 3.9%] as well as thyroid disease [5.8 %, 7.5 %, 9.2 %] was comparable in MND, sporadic ALS (sALS) and MS patients. Non-Statins [5.8 %, 3.9%] and Statins [17.1 %, 17.7%] use was comparable in MND patients compared with MS patients. Statin [17.1 %, 15.0 %, 17.7 %] use was comparable in sALS patients without DM/thyroid disease and PLS patients compared with MS patients. A significantly higher proportion of sALS patients with DM [45.5 %] used Statins compared with sALS patients without DM/thyroid disease or MS patients [17.1 %, 17.7 %]. Initiation of and discontinuation of Statins [27/41; 25/37; 3/23 (started-stopped/total-started)] was significantly more common in MND and sALS patients than MS patients [odds ratio – 12.9, 15.9 (95% confidence: 3.4–47.3, 4.1–59.8) $p < 0.00001$]. **Conclusions:** Reporting of Statin discontinuations in sALS patients is significantly more common than in MS patients and is not caused by reporting bias.

P7

**ALS, Physical Exercise, Trauma and Sports.
A Population-Based Pilot Case-Control Study**

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Torino, Bari, Milano and Foggia, Italy and Dublin, Ireland, and Preston, UK

Objective: To define the exposure to physical exercise in occupational and leisure activities (including professional sports) and to traumatic events in a representative sample of patients with amyotrophic lateral sclerosis (ALS) compared to the general population. **Background:** Several studies assessed the correlation between ALS, physical exercise and trauma with conflicting results, which may be explained by differing study populations and methods of assessment. **Methods:** Using population-based ALS registries located in Italy, the UK and Ireland, newly diagnosed patients with definite or probable ALS were enrolled. For each case, two age and sex-matched controls were selected from general practitioners' lists. Cases and controls were interviewed to have detailed information on occupations and sports. The source, intensity and duration of physical activity and the history of trauma (number, site, severity and complications) was also collected. The feasibility of the study was tested with a pilot investigation whose findings are presented here. **Results:** The sample included 61 cases (34M, 27F, age 33 to 86 years) and 112 controls (66M, 46F, age 30 to 84 years). The main occupation was blue-collar for 41.0% of cases and for 17.0% of controls ($p=0.001$). 13.1% of cases vs. 3.6% of controls reported strenuous physical activity at work ($p=0.05$). Compared to controls, patients with ALS had a longer exposure to work-related (10.7 vs. 7.3 years; $p=0.02$) and sport-related physical exercise (9.6 vs. 5.2 years; $p=0.005$). Three ALS patients (0 controls) reported professional sports ($p=0.04$). Traumatic events were fairly similar in cases and controls. After adjusting for gender, age and country, variables found to prevail in ALS patients were blue-collar occupation (OR 3.2; 95% CI 1.5–7.0), strenuous job (OR 3.8; 95% CI 0.9–15.2), and duration of sport-related physical exercise (OR 1.0; 95% CI 1.0–1.1). **Conclusions:** ALS is associated to physical exercise but not to traumatic events.

P8

A Population-Based Statewide Registry of Patients with Amyotrophic Lateral Sclerosis (ALS) in Massachusetts

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Objectives: Report the evolving methods and 2007 prevalence results of the Massachusetts statewide population-based registry of patients with ALS. **Background:** There are currently no population-based registries for ALS in the US. Since 2002, Massachusetts has been developing the tools to establish a statewide registry. Following completion of pilot studies, a registry of patients with

ALS was started on January 1, 2007. **Methods:** Case finding is mandated by state regulation and conducted annually. This report is of cases prevalent in 2007. Subsequent years will focus on incident cases. Primary data sources are 650 neurologists in private, clinic, or hospital practice and major hospital medical record departments. Secondary data sources include death certificates, hospices, and patient advocacy groups to determine if cases were missed. For each case reported, trained nurses abstract and collect a standardized set of clinical data. The diagnosis of ALS is confirmed and classified according to the revised World Federation of Neurology criteria for ALS by a neurologist experienced in applying these criteria (CA). **Results:** Collection of 2007 prevalent cases is complete. More than 87 percent of neurologists contacted responded to the call for cases. Case ascertainment through primary sources identified 519 potential cases with 216 reviewed thus far. Preliminary case verification classified 58% as definite, probable, or laboratory-supported probable ALS, 3% as possible, 22% as suspected, and 16% as not ALS. Approximately 180 additional potential cases not reported through the primary sources were identified from secondary sources; some may not have been prevalent in 2007. The verification review of all 699 potential 2007 cases will be completed in April. **Conclusions:** The successful development of the Massachusetts statewide registry presents researchers new opportunities for studying the occurrence of ALS. Challenges include sustainability and ensuring comparability with other surveillance datasets.

P9

**Study of Obesity as a Stroke Risk Factor in Chile.
A Case-Control Study**

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Santiago, Chile

Background: Sixty one per cent of the population in Chile is overweight and 23 % is obese. The prevalence increases with age and low socioeconomic status and is higher in women. **Objective:** To study if obesity measured by abdominal circumference (AC) and body mass index (BMI) is a risk factor for stroke. **Methodology:** Case control study. Cases: 104 patients over 40 years old with a first ischemic stroke diagnosed by CT or MRI. Controls: 104 inpatients without stroke, matched by sex and age. Weight, AC, BMI, hypertension, diabetes cholesterol levels, tobacco, physical activity, alcohol consumption, and family history of obesity were compared using t test, odd ratio (OR), logistic regression (LR) and ROC curves. **Results:** Mean age was 64.6 ± 10.9 y. Mean weight for cases was $73.8\text{Kg} \pm 11.8$ and $72.0\text{Kg} \pm 12.0$ for controls ($p=0.26$) and AC for cases was 967.0 ± 11.5 and 96.9 ± 11.0 for controls (OR=0.97, 95% CI= 0.93 to 1.02), $p=0.32$). Mean BMI was 27.3 ± 3.6 for cases and 27.6 ± 4.0 for controls (OR=1.16, 95% CI 0.94 to 1.18, $p=0.36$). LR analysis adjusted for hypertension, diabetes, blood cholesterol levels, tobacco and alcohol consumption, and coronary heart disease also showed that BMI and AC were not risk factors for stroke. This analysis showed that only hypertension (OR 3.0, 95% CI 1.4 to 6.4, $p=0.004$), blood cholesterol level (OR 2.1 95% CI 1.0 to 4.1, $p=0.04$), and tobacco (OR 2.4 95% CI 1.4 to 4.0 $p=0.001$) were significant risk factors for

ischemic stroke. ROC curves for AC and BMI showed that these measures did not predict stroke. **Conclusions:** Obesity studied by AC and BMI measures was not a risk factor for stroke in the present study.

P10

Current Depression in LGI1 Epilepsy Mutation Carriers

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Objective & Background: Depression is the most common comorbid psychiatric condition in individuals with epilepsy, but the cause is unknown. We addressed the role of shared genetic susceptibility in this comorbidity by investigating depression in families with a known genetic cause of epilepsy, i.e., mutations in the leucine-rich, glioma inactivated 1 gene (LGI1) autosomal dominant partial epilepsy with auditory features (ADPEAF). **Methods:** Administration of depression screen to 121 members of 11 families, each of which had a different mutation in LGI1. The family members were divided into three groups: affected carriers (n=47), unaffected carriers (n=10), and non-carriers (n=45). **Results:** Only two subjects, both affected carriers, met criteria for current *major depressive disorder*. Ten subjects met criteria for current *other depressive disorder*. Compared with unaffected carriers, the risk for current *other depressive disorder* was increased non-significantly in affected carriers (15.4% vs. 6.7%; OR=2.55, 95% CI=0.69–9.39) and in unaffected carriers (10.0% vs. 6.7%; OR=1.56, 95% CI=0.20–11.29). Current depression symptom scores were significantly higher in affected carriers than non-carriers (mean = 4.7 vs. 1.6, $p=0.002$) but were not increased in unaffected carriers (mean = 1.9 vs. 1.6, $p=0.85$). **Conclusions:** In this small study, current depressive symptom scores were higher in carriers of LGI1 mutations than non-carriers and this increase was restricted to carriers with epilepsy. Current *other depressive disorder* was more prevalent in affected and unaffected carriers compared to non-carriers but these differences were not significant. Our findings suggest that the increased rate of depressive symptoms in LGI1 mutation carriers with epilepsy is due either to a reaction to having epilepsy, depressogenic effects of epilepsy treatments or brain dysfunction induced by seizures. Future studies using a larger sample and assessing lifetime rather than current risk are needed to clarify whether or not depression is an alternative phenotypic manifestation of LGI1 mutations.

P11

Environmental Toxins and Risk of Narcolepsy among People with HLA DQB1*0602

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Objective: To examine the relation between environmental toxins and risk of narcolepsy among genetically susceptible individuals. **Background:** One etiologic model for narcolepsy suggests that some environmental toxin selectively and irreversibly destroys hypocretin-producing cells in the lateral hypothalamus in genetically susceptible individuals with HLA DQB1*0602. We examined narcolepsy risk in relation to toxins commonly found in jobs, hobbies and activities held by individuals with a genetic predisposition. **Methods:** We conducted a population-based case-control study in King County, Washington. Between 2001–2005, 67 prevalent cases were enrolled in the study, and 95 controls were recruited through random-digit dialing. Cases and controls were all between ages 18–50 and positive for HLA DQB1*0602. All were administered in-person interviews about jobs, hobbies or activities before age 21. All analyses were adjusted for African American race and income. Missing values on these covariates were multiply imputed before adjustment. **Results:** We observed a significantly increased risk associated with jobs involving heavy metals (OR=4.7; 95% CI: 1.5–14.5) and associations of borderline significance for those involving ceramics (OR=2.0; 95% CI: 0.9–4.7), pesticides (OR=2.1; 95% CI: 0.9–5.2), and paint (OR=1.7; 95% CI: 0.9–3.5). Significant associations were observed only at the highest exposure levels for hobbies and activities involving wood (OR=3.0; 95% CI: 1.0–8.9), fertilizer (OR=3.1; 95% CI: 1.1–9.1), and bug or weed killer (OR=4.5; 95% CI: 1.5–13.4). Significant dose-response relationships were evident for jobs involving metals ($p<0.03$) and paints ($p<0.03$), and for activities involving bug or weed killer ($p<0.02$). Restricting cases to those with cataplexy strengthened all associations except that for fertilizer. **Conclusions:** Toxins may play a role in the development of narcolepsy for those with a genetic susceptibility marker. Additional studies are needed to replicate the findings of these exploratory analyses and to continue the search for etiologic clues to narcolepsy.

P12

Self-Rated Health is an Independent Predictor for Mortality in the NEDICES Cohort

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Background: Self-rated health (SRH) is a predictor for mortality in several cohort studies. **Objective:** To evaluate SRH as a predictor for mortality in the elderly Neurological Disorders in Central Spain (NEDICES) cohort survey. **Methods:** The NEDICES cohort study evaluated the health status (subjective and objective) and the prevalence and incidence of several neurological disorders (dementia, Parkinsonism, essential tremor and stroke) in 5,278 participants in 1994–5 and 1997–8. The SRH was rated on a scale of five levels (from very good health to very poor health) in 4,958 participants in 1994–5 and 3,334 in 1997–8. The mortality of the cohort was evaluated by means of the Spanish National Registry on Mortality from 1994 to 2004. The relationships in the cohort between SRH (several neurological disorders participants included) and mortality were studied by Cox regression analysis adjusted by age, sex, education level and co-morbidity. **Results:** To have less than good SRH (*fair*, HR=1.26, CI95%=1.02–1.54; *poor*, HR 1.50, CI95%=1.30–1.90; *very poor*, HR=1.60; CI95%=1.10–2.30) in the baseline survey had higher mortality than to have good or very good SRH. Also, 1,786 participants had worse SRH in the incidence survey (1997–8) than in the baseline survey and they had higher mortality at 2004 (HR=1.47; CI95%=1.21–1.78). Participants with the neurological disorders evaluated, mainly demented and Parkinson disease sufferers, had worse SRH than the rest of the cohort and greater mortality. **Conclusions:** Baseline SRH status and its worsening is an independent predictor for mortality. Participants with the neurological disorders evaluated had worse SRH than the rest of the cohort and greater mortality.

P13

Cholesterol-Lowering Drugs and Risk of Amyotrophic Lateral Sclerosis: A Population-Based Case-Control Study

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Objective: To determine whether the use of statins or other cholesterol-lowering medications increases the risk of developing amyotrophic lateral sclerosis (ALS). **Background:** Statin treatment has been associated with muscle-related pathology including myalgias, myopathy, and rhabdomyolysis. Recent international drug safety monitoring reports and data mining signals from the FDA's Adverse Event Reporting System indicate that statins are reported in combination with ALS 1.6–8.5 times more frequently than expected in comparison to other medications, however, an analysis of existing statin clinical trial data did not support an association. **Methods:** We identified 190 incident cases of ALS that were newly diagnosed during 1996–1999 among members of the Kaiser Permanente Northern California health maintenance organization. We selected 10 age-, sex- and membership-date-matched controls for each case. We linked information on ALS cases and control subjects to computerized pharmacy records containing information on the prescription of cholesterol-lowering medications. Odds ratios for the association between cholesterol medication use and ALS were estimated using logistic regression with adjustment for age, sex, and membership dates. **Results:** A higher percentage of ALS cases (28/190; 14.7%) than controls (161/1900; 8.5%) had used statin medications prior to the diagnosis of ALS (or index date for controls). The age- and sex-adjusted odds ratio (OR) for statin use was 1.9 (95% CI 1.2–2.9; $p=0.005$), and there was a significant positive trend with increasing duration of statin use ($p=0.01$). Adjustment for other comorbid conditions and health utilization indices did not alter the association. Treatment with other cholesterol-lowering medications including bile acid sequestrants and fibrates was not significantly associated with ALS. **Conclusions:** We found that statin medication use is associated with an increased risk of ALS, with a dose-response trend with duration of treatment. If confirmed in other studies, this finding could contribute to knowledge about the pathogenic mechanisms of ALS.

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