

confined in several occupations. Thus, we aimed to evaluate PAHs exposure across a wide range of occupations using its urinary metabolite 1-hydroxypyrene (1-OHP).

**Methods** To evaluate PAHs exposure across occupations, we collected the urine 1-OHP data from the Korean National Environmental Health Survey which is a nationwide bio-monitoring survey. The data contained information about urine 1-OHP levels, cigarette smoking status, and standard occupational codes. We calculated summary statistics of urine 1-OHP levels for each occupation. In addition, we calculated the relative exposure indicators which are the proportions of exceeding the quartile levels. Since cigarette smoking is a single most influential factor of PAHs exposure, we repeated the analyses by excluding current smokers.

**Results** Overall geometric means (GM) of all populations and non-smoker populations were 0.13 $\mu$ g/L and 0.10 $\mu$ g/L, respectively. For the major group of occupation, 'Craft and Related Trades Workers' and 'Equipment, Machine Operating and Assembling Workers' showed the highest urine 1-OHP levels, while 'Homemaker' showed the lowest level. For the sub-major group of occupation, 'Video and Telecommunications Equipment Related Occupations' showed the highest percentage (61%) of exceeding the third quartile (Q3) level of all populations. While 'Legal and Administration Professional Occupations' showed the lowest percentage of exceeding the Q3 level of all populations. For the minor group of occupation, 'Horticultural and Landscape Workers' showed the highest percentage (64%) of exceeding the Q3 level of all populations. While 'Kindergarten teachers' showed the lowest percentage of exceeding the Q3 level of all populations.

**Conclusions** Our results will provide ancillary information about PAHs exposure across occupations, especially in occupations where PAHs exposure has not well known.

#### 06D.4 ASSOCIATION OF OCCUPATIONAL EXPOSURES WITH EX VIVO FUNCTIONAL IMMUNE RESPONSE IN WORKERS HANDLING CARBON NANOTUBES AND NANOFIBERS

<sup>1,2</sup>Mary Schubauer-Berigan\*, <sup>2</sup>Matthew Dahm, <sup>3</sup>John Beard, <sup>4</sup>Vamsi Kodali, <sup>4</sup>Patti Zeidler-Erdely, <sup>4</sup>Aaron Erdely. <sup>1</sup>International Agency for Research on Cancer, Lyon, France; <sup>2</sup>National Institute for Occupational Safety and Health, Cincinnati, USA; <sup>3</sup>Brigham Young University, Provo, USA; <sup>4</sup>National Institute for Occupational Safety and Health, Morgantown, USA

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Animal toxicology studies suggest that workers exposed to carbon nanotubes or nanofibers (CNT/F) may experience pulmonary or systemic health effects; however, direct human evidence is lacking. Our study's objective was to evaluate associations between CNT/F exposure and *ex vivo* responses of leukocytes challenged with secondary stimulants, adjusting for potential confounders, in a cross-sectional study. We measured multi-day exposure using CNT/F structure count (SC) and elemental carbon air concentrations among 102 U.S. workers. Demographic, lifestyle, and other occupational information was obtained via in-person interview. Workers' whole blood was incubated for 18 hours with and without two microbial stimulants

(lipopolysaccharide and staphylococcal enterotoxin type B) using TruCulture<sup>®</sup> technology to evaluate immune cell activity. Following incubation, collected supernatants were preserved and subsequently analyzed for cytokine and chemokine concentrations. The ratio of stimulant:null response for each protein was analyzed using multiple linear regression, principal components (PC) analysis, and Ingenuity<sup>®</sup> Pathway Analysis (IPA) to determine whether patterns of protein response were associated with CNT/F exposure. We found that CNT/F metrics (most consistently, the SC-based) were significantly ( $p < 0.05$ ) inversely associated with stimulant:null ratios of GM-CSF, IFN- $\gamma$ , interleukin (IL)-2, IL-4, IL-5, IL-10, IL-17, and IL-23. CNT/F metrics were significantly inversely associated with PC1 (a weighted mean of most biomarkers that explained 25% of the variance in the set of protein ratios) and PC2 (a biomarker contrast that explained 14%). Among other occupational exposures, only solvent exposure was significantly (and was inversely) related to PC2. IPA suggested a CNT/F-associated generalized inhibition of all leukocyte responses when challenged with a secondary stimulus. We found that CNT/F exposure metrics were uniquely related to a pattern of reduced stimulant responses in challenged circulating leukocytes. This approach, if replicated in other exposed populations, may present a relatively sensitive method to evaluate human response to CNT/F or other occupational exposures.

#### 06D.5 ELECTRONIC WASTE RECYCLING EXPOSURE AND HORMONE LEVELS IN WORKERS

<sup>1,2</sup>Sabrina Gravel, <sup>2</sup>Bouchra Bakhiyi, <sup>2,3</sup>Jérôme Lavoué, <sup>2</sup>Marc-André Verner, <sup>2</sup>Joseph Zayed, <sup>1,2</sup>France Labrèche\*. <sup>1</sup>Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), Montreal, Canada; <sup>2</sup>Dept. Environmental and Occupational Health, School of Public Health, University of Montreal, Montreal, Canada; <sup>3</sup>Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM), Montreal, Canada

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**Background and objective** Electronic waste recycling (e-recycling) exposes workers to several contaminants, including flame retardants that are suspected endocrine disruptors. We aimed to explore the association between polybrominated diphenyl ethers (PBDEs) and hormone levels in the serum of Canadian e-recycling workers.

**Methods** In a cross-sectional study, blood samples were collected from 85 e-recycling workers (six facilities) and from 15 workers in other types of recycling (two facilities), at the end of a work shift. Socio-demographic information was obtained by questionnaire and body mass index (BMI) was calculated from measured height and weight. Serum concentrations of 13 PBDE congeners were measured as well as thyroid hormones (free and total thyroxine [T4], triiodothyronine [T3], thyroid stimulating hormone [TSH]) and testosterone (free and total). Linear regressions were stratified on sex and adjusted for age, BMI, seniority, smoking status, and type of recycling. Ten participants were excluded because of thyroid or testicular problems.

**Results** Participants were 23 women and 77 men (mean 40 years old, SD=12 years). Average hormone levels were within the laboratory normal range. In e-recycling, geometric mean concentrations of the most detected congeners were 11, 11 and 20 ng/g lipids for BDE47, BDE153 and BDE209, respectively. Only BDE209 concentrations were higher in e-recycling than in the control group. A two-fold increase in serum

BDE209 was associated with a significant increase of 2.48 nmol/L in total T4 in men ( $p=0.011$ ), and with a close to significant increase in the free/total testosterone ratio of 6% in men ( $p=0.053$ ). BDE47 and BDE153 were not associated with hormone levels.

**Conclusions** The clinical significance of high exposure to BDE209 in working adults is yet to be established, but endocrine effects were observed in this population. E-recycling workers are highly exposed to PBDEs among other substances, which may make them more vulnerable to hormonal disruption.

## Mini-Symposium 4: Advances in Neurodegenerative Disease Epidemiology

### 06E.1 SELF-REPORT OCCUPATIONAL EXPOSURES AND MND IN NEW ZEALAND

<sup>1</sup>Grace Chen\*, <sup>1</sup>Andrea 't Mannetje, <sup>1</sup>Jeroen Douwes, <sup>2</sup>Leonard van den Berg, <sup>1</sup>Dave McLean, <sup>3</sup>Neil Pearce, <sup>4</sup>Hans Kromhout, <sup>5</sup>Wendyl D'Souza, <sup>6</sup>Melanie McConnell. <sup>1</sup>Centre For Public Health Research, Massey University, Wellington, New Zealand; <sup>2</sup>Brain Centre Rudolf Magnus, Department of Neurology, University Medical Centre, Utrecht, The Netherlands; <sup>3</sup>Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK; <sup>4</sup>Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands; <sup>5</sup>Department of Medicine, University of Melbourne, Melbourne, Australia; <sup>6</sup>School of Biological Sciences, Victoria University, New Zealand

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**Background** We have reported previously the results on a New Zealand population based case-control study evaluating occupations as risk factors for MND. The aim of this study was to investigate the associations between 11 different occupational exposure groups and the risk of MND by using self-reported job-related exposures.

**Methods** We recruited 321 cases through the New Zealand Motor Neurone Disease Association and hospital discharges records, and 605 population controls from the Electoral Roll between 2013 and 2016. A standardized questionnaire was used to obtain information on personal and demographic details, lifestyle factors and a full occupational history with detailed workplaces exposures. Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals for MND. Analyses were adjusted for age, gender, ethnicity, socioeconomic status, education and smoking.

**Results** Significantly elevated risks for MND were observed for self-reported job related exposures to Fibres (OR=1.39, 95% CI 1.00–1.93); Fumigants (OR=2.44, 95% CI 1.35–4.23); Animal and Animal Products (OR=1.41, 95% CI 1.03–1.92); Other Chemicals (OR=1.53, 95% CI 1.14–2.05) and Fungicides/Insecticides/Herbicides/Timber Preservatives (OR=1.44, 95% CI 1.05–1.99)

**Conclusions** Our study shows various occupational related exposures with increased odds of MND. While study results need to be interpreted cautiously given the lack of direct exposure measures, these results, in particular exposure to Fumigants, Fungicides/Insecticides/Herbicides/Timber Preservatives which were consistent with our previous results on agriculture occupations and MND risk. Future studies will have a particular focus on exposures specific for certain job tasks and dose-response relationships.

### 06E.2 EXPOSURE ASSESSMENT FOR A STUDY OF COGNITIVE IMPAIRMENT IN FORMER PROFESSIONAL FOOTBALLERS IN ENGLAND

<sup>1</sup>Damien Mcelvenny\*, <sup>1</sup>Ioannis Basinas, <sup>1</sup>Richard Graveling, <sup>1,2</sup>John Cherrie, <sup>3</sup>Valeentina Gallo, <sup>4</sup>Simon Kemp, <sup>5</sup>Neil Pearce. <sup>1</sup>Institute of Occupational Medicine, Edinburgh, UK; <sup>2</sup>Heriot-Watt University, Edinburgh, UK; <sup>3</sup>Queen Mary, University of London, London, UK; <sup>4</sup>Rugby Football Union, London, UK; <sup>5</sup>London School of Hygiene and Tropical Medicine, London, UK

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Evidence is accumulating on the possible increased risks of neurodegenerative disease in former (professional) sportspersons. This study will assess the associations between a history of repetitive low-level head trauma and general and neurological health in retired professional footballers aged 50+ in England. The main exposure measures are concussions and cumulative lifetime repeated sub-concussive head impacts (RSHIs), either from heading footballs or other forces applied to the head. Information on factors associated with concussions and RSHIs will be collected via a structured questionnaire during face-to-face interviews.

Our approach will include:

- Literature search to identify potentially important proxy measures of RSHI during training and matches;
- Developing a model of cumulative RSHIs, based on the more strongly predictive variables, which may include playing position, the frequency of heading, the number of games played and training sessions attended, decade of play and the type of ball used.
- The model will be developed from analyses of head contacts from video footage of matches and training, at the individual level and in general, and from statistics on playing career. We will also consult a panel of former professional footballers on the exposure assessment.

The exposure data will be crucial to assess whether those with higher exposure within the study cohort are at increased risk compared to those with lower exposure.

### 06E.3 CAN THE MULTISTAGE MODEL BE APPLIED TO AMYOTROPHIC LATERAL SCLEROSIS (ALS)?

Neil Pearce. London School of Hygiene and Tropical Medicine, London, UK

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**Background** There are several intriguing features of amyotrophic lateral sclerosis (ALS). Some people with genetic susceptibility never develop ALS; ALS develops in late life and progresses rapidly; the same mutation can predispose to ALS or other diseases; ALS starts in one region and spreads; degeneration is specific to a subgroup of neurons; and ALS shows complex inheritance. Cancer shares many of these characteristics, and these have been incorporated into the Armitage-Doll multistage model. We therefore used this model to investigate the hypothesis that ALS is a multistage process.

**Methods** Incidence data by age and sex were generated from five ALS population registers, in Ireland, the Netherlands, Italy, Scotland and England; age and sex adjusted incidences were calculated for each register.