O-058

Against Programming Patrick Bateson, *Sub-Department of Animal Behaviour, University of Cambridge, High Street, Madingley, Cambridge CB3 8AA, UK*

Different adaptive phenotypes arising from a common genotype are reported with ever increasing frequency. In these examples of developmental plasticity an environmental condition or maternal state commonly establishes a particular trajectory of development in early life. Unfortunately, the terminology for these processes has become confused. To call them "programming" is somewhat similar to saying that pressing a button on a juke box is "recording" the tune. Misleading metaphors in science matter if they confuse or send research off in unprofitable directions. Some signs suggest that this has already happened with programming. A reputable and long-established term from developmental biology that would do instead is "induce" but a perfectly good neutral word would be "elicit" which might produce a graded or a discrete response. With this confusion cleared up, a distinction could then be drawn between developmental process and developmental outcome. The outcome could be described, if you must, as "programmed by Darwinian evolution" but not by the conditions of early life. Could we use this conference to clean up our act?

O-059

Prenatal Restraint Stress and Behavior in Fischer 344 Rats; The Implications of a Subsequent Exposure to Stress Daniël L.A. Van den Hove*/**, Harry W.M. Steinbusch**, Matteo Bruschettini*/**, Hellen Steinbusch*/**, Jos Prickaerts**, Carlos E. Blanco*, *Pediatrics/GROW, **Psychiatry and Neuropsychology/Brain and Behavior (EURON), Maastricht University, 6200 MD Maastricht, Netherlands.

Background: In recent years, there has been increasing awareness that chronic exposure to stress during prenatal development can predispose progeny to various psychological disorders in adulthood. However, recent findings in Fischer 344 rats suggested that an adaptive or protective effect of prenatal stress (PS) towards stress should not be excluded. **Objective**: Our main objective was to examine the effect of a subsequent stress exposure on anxiety and depressive-like behavior in PS and control rats. **Design/Methods**: During the last week of gestation (E14-E21) pregnant female Fischer 344 rats were individually restrained in transparent plastic cylinders (for three 45 min periods per day), while, in addition, being exposed to bright light. Control dams were left undisturbed. To examine the effect of a subsequent exposure to stress male PS and control offspring were exposed to a 3-day period of stress (mouse cage/restraint stress/wet bedding) at an age of 3 months. Anxiety and depressive-like behavior of the rats was tested both before and at an age of 6 months. In addition, stress-induced plasma corticosterone secretion and cell proliferation within the hippocampal dentate gyrus (DG) was studied. **Results**: We found PS animals to weight less at birth as compared to control offspring. Further, PS rats were more anxious before the subsequent exposure to stress, as measured in the open field and home cage emergence tasks, whereas, afterwards, they performed relatively better, i.e. they were less anxious, as compared to controls in these tasks. In addition, PS animals initially exhibited more depressive-like behavior, as measured in the forced swim test, which normalized after the subsequent exposure to stress. No differences were observed in stress-induced plasma corticosterone secretion and cell proliferation within the DG. **Discussion**: Our data are in support of 'predictive adaptive response' (PAR) hypothesis, which predicts that PS allows offspring to better cope with stress in later life as compared to offspring that developed under 'normal' prenatal conditions. In conclusion, PS Fischer 344 rats seem to perform relatively better under stressful conditions as compared to control rats. The present data provide further evidence for the idea that PS may also have, dependent upon the genetic background and history, adaptive and/or protective properties. Finally, this study once more underlines the importance of the choice of strain in stress-related investigations.

Parallel Session 4D: Developmental Disruption

O-060

Traffic Polycyclic Aromatic Hydrocarbons (PAHs) Genetic Susceptibility and Risk of Breast Cancer Jing Nie, Jan Beyea, Matthew Bonner, Daikwon Han, John Vena, Peter Rogerson, Dominica Vito, Paola Muti, Maurizio Trevisan, Peter Shields, and Jo Freudenheim; Department of Social and Preventive Medicine, State University of New York at Buffalo, Buffalo, NY, Consulting in the Public Interest, Lambertville, NJ, University of South Carolina, Columbia, SC, Georgetown University, Washington, DC, USA

Background: Growing evidence suggests that there may be critical time periods of exposure in breast cancer initiation and development. Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous and exist in the ambient environment at low levels. We previously found evidence that exposure to PAHs based on an estimate of exposure to traffic emissions in a woman's earlier life may be associated with breast cancer risk in adulthood. Glutathione S-transferase mu, a phase II enzyme, is involved in the detoxification of PAHs. There is a common *GSTM1* genetic polymorphism that is a deletion of the entire gene. The *GSTM1* null genotype is associated with a deficient detoxifying enzyme activity. In this study, we examined the association between *GSTM1* genotypes and breast cancer risk, and interaction with traffic emission-PAH exposure estimated for each woman at menarche, at the time when she had her first birth, and at 20 and 10 years prior to interview, using data collected from the Western New York Exposures and Breast Cancer (WEB) study, a population-based case control study. **Methods**: All participants were women, aged 35-79, residents of Erie and Niagara Counties. Cases had incident, primary, histologically-confirmed breast cancer. Controls were randomly selected and frequency-matched to cases on age, race and county. In-person interviews were used to collect data on potential breast cancer risk factors including self-reported lifetime residential history. Blood samples were collected at the time of the interview and used to determine *GSTM1* genotype. A geographic model was used to reconstruct historical traffic PAH exposure at each residence. **Results**: There was no main effect of *GSTM1* on breast cancer risk. While we had previously found an association between higher exposure to traffic emission PAHs and breast cancer risk, we now found evidence that the association was limited to women with *GSTM1* null genotype. For exposure at menarche, limited to women living within 250 meters of a road with traffic counts, the upper quartile of PAH exposure was associated with increased risk of premenopausal breast cancer (OR 4.64, 95% CI 0.98-21.94; p for trend 0.01) and emissions at the time of a woman's first birth was associated with increased risk of postmenopausal breast cancer (OR 3.27, 95% CI 0.99-10.84, p for trend 0.02). There was no association of traffic emissions with risk among women with *GSTM1* wild-type, or for any of the other time periods. **Conclusions**: Our findings suggest that there is increased risk of breast cancer associated with exposure to traffic emission PAHs in early life, and that the association is limited to women with *GSTM1* null genotype.

O-061

Maternal Alcohol Ingestion during Pregnancy Predisposes to Smaller Kidneys and Albuminuria in Aboriginal Children: Findings from an Aboriginal Birth Cohort Gurmeet R. Singh[1], Susan M. Sayers[1] and Wendy E. Hoy[2]; [1] *Public Health and Chronic Disease Division, Menzies School of Health Research and Charles Darwin University, Darwin, Australia.* [2] *Centre For Chronic Disease, University Of Queensland, Brisbane, Australia*

Aim: To examine the relationship of maternal smoking and alcohol use during pregnancy to kidney size and function in c0hildhood, in birth cohort of Australian Aboriginal children. **Background:** It has been proposed that intra-uterine growth retardation causes impaired nephrogenesis resulting in lower nephron numbers and smaller kidneys. This effect could be mediated either directly or via exposure to distal factors such as poor maternal nutrition and/or exposure to alcohol and nicotine during critical periods of renal development. **Methods:** A longitudinal prospective study of an Australian Aboriginal birth cohort (n=686) established between 1987 and 1990 formed the study population. Post-natal maternal weight and height and self reported smoking and alcohol use, and birth size was recorded at the time of birth. Clinical gestational age was assessed within 4 days of birth using the Dubowitz method as last menstrual period (6.5 %) and early sonograms for dating of pregnancy (8.2 %) were rarely available. Wave 2 follow-up at age 8-14 years (mean age 11.5 years) on 572 children included an assessment of kidney function using urine albumin creatinine ratios (ACR; n=533) and an estimation of renal size by ultrasound measurements(n=529). For analysis, kidney volumes corrected for current body surface area (BSA) were divided into quartiles. **Results**: In this cohort, 56% (375/667) of the mothers smoked and 13.6% (88/649) consumed alcohol during pregnancy. Mothers who smoked were more likely to have for small-for-gestational age babies (SGA; OR 1.5, $p < 0.03$). Alcohol use during pregnancy was not associated with either SGA or preterm babies. Antenatal alcohol exposure was associated with a significantly higher proportion of children with pathological albuminuria (= 3.4) adjusted for age, sex and weight; 14.5% compared to 6.5% (p=0.03). Corrected kidney volumes in the lowest quartile were more common in those exposed to alcohol in utero (40% compared to 22%: p=0.003), and the association persisted after adjustment for the effect of SGA, maternal smoking and maternal BMI. Stratification of results by in utero exposure to smoking alone, alcohol alone or exposure to both revealed the same trends, although the numbers of mothers who consumed alcohol but did not smoke were small. **Conclusion**: Alcohol exposure in utero has an adverse effect on renal size and function during childhood. Alcohol consumption during pregnancy may be one of the contributors to the multi-determinant renal disease currently present in epidemic proportions Australian Aboriginal people living in the Northern Territory of Australia.

O-062

Neonatal Exposure to the Phytoestrogen Genistein Adversely Affects Fertilization Rate and Oocyte Quality Later in Life Wendy N. Jefferson[1,3], Elizabeth Padilla-Banks[1], Eugenia H. Goulding[2], E.M. Eddy[2] and Retha R. Newbold[1]; [1]*Developmental Endocrinology Section, Laboratory of Molecular Toxicology, and* [2]*Gamete Biology Section, Laboratory of Reproductive and Developmental Toxicology, NIEHS, NIH, DHHS, RTP, NC 27709 and* [3]*Department of Environmental and Molecular Toxicology North Carolina State University, Raleigh, NC 27605*

Background: Exposure of the developing organism to estrogenic substances is known to cause deleterious effects on the reproductive tract. Previous studies have shown that neonatal exposure to the naturally occurring phytoestrogen, genistein (Gen) causes adverse consequences on the developing female reproductive system. Gen alters ovarian development and function as well as causes infertility and uterine cancer later in life. We have shown that Gen alters ovarian differentiation by preventing the breakdown of oocyte nests during the first week of life, thus resulting in multi-oocyte follicles (MOFs); these effects are mediated through estrogen receptor (ER) ß. To