Published in final edited form as:

Alcohol. 2013 December ; 47(8): . doi:10.1016/j.alcohol.2013.09.042.

A report on the Fetal Alcohol Spectrum Disorders Study Group meeting of 2012, Theme title, “*Biomarkers for FASD*”

Rajesh C. Miranda¹, Julie Kable², James N. Reynolds³, and C. Fernando Valenzuela⁴

¹Dept. Neuroscience and Experimental Therapeutics, Texas A&M Health Science Ctr., Bryan, TX

²Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA

³Department of Biomedical and Molecular Sciences, Queens University, Kingston, Ontario, Canada

⁴Dept. of Neurosciences, School of Medicine, University of New Mexico HSC Albuquerque, NM

Abstract

The 2012 meeting of the Fetal Alcohol Spectrum Disorders Study Group (FASDSG) focused on the development and ethics of biomarkers for fetal alcohol exposure. This one-day international conference brought students and trainees together with clinicians and researchers to discuss the latest research on FASD. One keynote speaker discussed the value of profiling epigenetic modifications in readily available fetal tissues to diagnose fetal exposure to environmental agents, while the second speaker discussed the ethics of biomarker development within the context of core principles of justice, autonomy, beneficence and non-maleficence. Three sessions of short data talks informed the audience of research advances with particular emphasis on the diagnosis of FASD. Other activities included updates on FASD-related activities by representatives of government agencies, a report on the implementation FASD-related diagnostic criteria in the fifth edition of the Diagnostic and Statistical Manual (DSM-5) of the American Psychiatric Association and a networking lunch, and the presentation of the “Merit Award” to Dr. Nathan Muraski for his work on behavioural outcomes of fetal alcohol exposure. The capstone of the meeting was the presentation of the “Henri Rosett” award to Dr. Denis Viljoen, in recognition of his role in raising awareness about the incidence of FASD in South Africa and in promoting FASD prevention and treatment programs as chairperson and chief executive officer of the Foundation for Alcohol Related Research (FARR).

Keywords

Fetal Alcohol Spectrum Disorder; epigenetics; biomarker; ethics; Rosett Award

The 2012 meeting of the Fetal Alcohol Spectrum Disorders Study Group (FASDSG), held in San Francisco, CA included a total of 190 attendees. Of these, 42 were students/trainees. Twelve students received travel awards to present their research at FASDSG and to attend the subsequent Research Society on Alcoholism meeting. Countries represented included Argentina, Canada, France, Japan, New Zealand, Norway, South Africa, Turkey, and the

© 2013 Elsevier Inc. All rights reserved.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

USA. During the course of the meeting, attendees learned about new directions in research on FASD from two keynote speakers as well as fourteen short research presentations by the membership. Eleven of the short presentations were made by students or post-doctoral fellows. A timely update on the newest revision of the Diagnostic and Statistical Manual, Fifth Edition (DSM-5) of the American Psychiatric Association was also presented. Aside from research presentations, attendees received updates on FASD-related activities from the National Institute on Alcohol Abuse and Alcoholism (NIAAA), Centers for Disease Control and Prevention (CDC), the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD) and from the Substance Abuse and Mental Health Services Administration (SAMHSA) FASD Center of Excellence. Attendees also participated in a networking lunch, which gave student attendees the opportunity to interact with more senior researchers and clinicians. The capstone of the meeting was the presentation of the Merit award to recognize an outstanding young researcher, and the Rosett Award, to recognize the lifetime achievement and service towards eradication of FASD.

Keynote Presentations

The theme of the 2012 meeting of the FASDSG, “Biomarkers for FASD”, focused on identifying promising approaches for, as well as the ethics of developing biomarkers for FASD. The rationale behind the focus on biomarkers for FASD is that fetal exposure to ethanol does not result in characteristic craniofacial dysmorphism or growth deficiency in all cases. Indeed, the presence of craniofacial dysmorphism detects only the severest instances of fetal alcohol exposure. Moreover, a confirmed history of prenatal ethanol exposure is frequently absent, making a definitive diagnosis difficult in many cases. Therefore, there is a significant need to identify alternate biomarkers of ethanol exposure at stages of both fetal and child development that will aid in the identification of children at risk. The meeting also addressed the issue that the need for good biomarkers has to be balanced with the significant ethical, biomedical and legal implications associated with the use of biomarkers to make a medical diagnosis of fetal alcohol exposure. There is a very real possibility that such a diagnosis will generate unintended legal and economic consequences for the birth mother as well as for the child. *The keynote presentations contrasted the future promise and risks associated with biomarker development.*

The first keynote presentation by Dr. Robert Wright, Harvard Medical School and School of Public Health, was entitled, “*Epigenetics and Reproductive Health*”. Dr. Wright presented data from two human studies, the Early Life Exposures in Mexico and Environmental Toxicology (ELEMENT) longitudinal birth cohort in Mexico City, and the Metals Assessment Targeting Community Health (MATCH) study in Tar Creek, Oklahoma, assessing the role of environmental chemicals on child health and development. This presentation touched on the fact that a variety of agents including maternal tobacco smoke exposure, social stress, lead exposure, air pollution as well as ethanol are risk factors for impaired fetal growth. In recent years, a growing body of literature has demonstrated that all of the risk factors for impaired fetal growth can also alter DNA methylation, suggesting a common pathway by which environmental factors impair fetal growth. Vascular system tissues including blood cells, blood vessels like umbilical arteries and veins, as well as the placenta are important for fetal growth and are logical target tissues for environmental agents. Furthermore, these tissues are readily accessible at birth and can therefore be harvested to assess the presence of ‘biomarkers’ for environmental exposures. In assessing DNA methylation patterns in vascular tissues, Dr. Wright’s presentation focused on the use of “methyloomics” in umbilical cord vessels as a biomarker for fetal growth restriction associated with multiple environmental agents. He presented data showing that environmental agents can influence tissue methylation patterns, but that the effect of the environment on methylation patterns of many genes is tissue-specific. When comparing low

to normal birth-weight children, DNA methylation responses in blood, umbilical artery and umbilical vein differ from each other. Therefore, while gene methylation patterns in each of these tissues may be used as a marker for exposure, they may have limited value in terms of assessing the effects of exposure on other target tissues like the brain. However, other genomic elements including repetitive elements, retro-transposons and imprinted genes (wherein one parent-of-origin allele is silenced while the allele derived from the other parental genome is transcribed), are expected to exhibit similar methylation patterns across tissue and their assessment may permit inferences about the effects of environmental agents on other tissues including the brain. Loss of imprinting in particular is associated with fetal growth retardation or overgrowth syndromes, and therefore assessment of the imprinted status of these gene loci is likely to be particularly informative about child development and health (Fleisch et al., 2012).

The development of biomarkers for maternal drug exposure is fraught with significant ethical and legal issues that merit analysis and discussion before these biomarkers are broadly adopted. Therefore, the second keynote presentation, entitled, “*Ethical considerations in screening for biomarkers related to prenatal exposure to alcohol*”, was delivered by Dr. Nina Di Pietro, National Core for Neuroethics, The University of British Columbia, Canada. Although current biomarkers of prenatal alcohol exposure remain limited in their predictive and diagnostic power, progressive technological advancements in alcohol research will continue to improve their accuracy and clinical utility. While screening may offer opportunities for early intervention, many complicated ethical issues must be considered, including the potentially stigmatizing effects of targeted vs. population screening, the legal and personal ramifications of a positive test result, understanding the limitations of screening with regard to diagnosis of FASD, and the implications for maternal rights and decision-making. Dr. Di Pietro introduced the topic with a Canadian case report that served as an example of the intersection between medical and legal decisions about childcare associated with the diagnosis of drug exposure. In a follow-up, she used perinatal meconium screening as an example of a source of a variety of biomarkers. An important point that was raised is that biomarker tests may result in both false-positive or false-negative outcomes, each of which could result in important negative consequences such as failure to provide services, or emotional distress and the inappropriate referral to child protective services. Dr. Di Pietro also discussed the core principles of bioethics, i.e., justice, autonomy, beneficence and non-maleficence. The bioethical principle of justice, i.e. the obligation to be fair in the distribution of risks and benefits, may be served by implementing universal screening. The principle of autonomy would be served by strong protections for the rights to informed consent and refusal to participate in testing. The principle of beneficence would be served if testing were a gateway to social and medical services, while the principle of non-maleficence would be served by limiting harm (e.g., punitive legal consequences). Evidence indicates support for universal screening under the above principles, and in the Canadian health care system, projected savings per quality-adjusted life year would justify the additional costs of routine testing. Finally, the limitations to the practice of bio-ethical principles were discussed, including practical limitations of ‘opt-in’ vs. ‘opt-out’ screening protocols, the inadequacy of counselling and disclosure practices in the medical system, limited access to services and tension in the medical-legal profession between punitive and non-punitive approaches subsequent to diagnosis (Zizzo et al., 2013).

These keynote presentations were followed by a spirited and open discussion moderated by Dr. Cynthia Bearer, University of Maryland School of Medicine. The discussion reinforced the need for careful ethical consideration of the adoption of biomarkers for screening for fetal alcohol exposure, before such screening becomes more sophisticated (such as the approaches outlined by Dr. Wright) and universal.

Update on DSM-5

Dr. Julie Kable (Emory University School of Medicine) provided an update to the membership regarding efforts by the Alcohol Related Neurodevelopmental Disorder (ARND) workgroup from the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD), to include a disorder, titled Neurobehavioral Disorder Associated with Prenatal Alcohol exposure (ND-PAE) in DSM-5. In addition to Dr. Kable, membership on the ARND workgroup included (in alphabetical order), Dr. Sally Anderson (NIAAA, NIH), Dr. Heather Carmichael Olson (University of Washington), Dr. Sarah Mattson (San Diego State University), Dr. Mary O'Connor (University of California at Los Angeles), Dr. Blair Paley (University of California at Los Angeles), Dr. Edward Riley (San Diego State University), and Dr. Kenneth R. Warren (NIAAA, NIH). The ARND workgroup proposed including the ND-PAE category in DSM-5 to address three identified problems: (1) there is no specific mental health code that adequately documents the cognitive and mental health impact of PAE, (2) children with FASD may not respond to treatment regimens developed using the existing codes, which may lead to inappropriate treatments, and (3) when seeking mental health care (assessments or interventions), providers and families often struggle with obtaining appropriate reimbursement for habilitative care. The ICCFASD-ARND workgroup in collaboration with Dr. Bridget Grant (NIAAA, NIH) and the DSM-5 Substance-Related Disorders Work Group revised the diagnostic criteria and introductory pre-text, prepared a memo to the APA Board of Trustees justifying the addition of the disorder, and revised a white paper summarizing scientific evidence supporting the cluster of symptoms proposed as criteria for the disorder and the evidence differentiating this disorder from other psychiatric disorders already in existence. The proposed disorder was being considered for *Section III: Disorders in need of further study* of the DSM-5 and the criteria were posted for public comment on the APA website. To meet the criteria for diagnosis of ND-PAE, the ARND workgroup proposed that a history of more than minimal exposure to alcohol be documented, along with impairments in three domains of behavioral functioning: neurocognitive impairment, self-regulation, and adaptive functioning.

FASt data presentations

Fourteen abstracts submitted by FASDSG members were selected to provide brief 5-minute presentations of their cutting edge new research findings using one slide. Three of these were given by senior investigators and eleven by students and postdoctoral researchers, providing a showcase for the organization's young researchers. The presentations were divided into three thematically organized sessions with the first entitled "Pathophysiology and Effect Modifiers," the second "Neurodevelopmental Impact of Prenatal Alcohol Exposure (PAE)," and the third "Biomarkers of Fetal Alcohol Spectrum Disorders (FASD)."

FASt Data Presentations I: Pathophysiology and Effect Modifiers

(Presenter's name is indicated in bold font)

Xiaopan Chen, Jie Liu, and Shao-yu Chen (University of Illinois College of Medicine) explored mechanisms involved in apoptotic cell death, particularly the role of MicroRNAs (miRNAs). Modulation of ethanol-induced apoptosis in neural crest cells by miR-125b was explored using mouse embryos exposed to ethanol in vivo or in whole embryo cultures. Findings indicated that miR-125b prevented ethanol-induced apoptosis and that microinjection of an miRNA mimic prevented ethanol-induced embryo toxicity. They suggested that miRNAs should be considered as a possible novel therapeutic strategy for the prevention of FASD.

Shane Huebner, B. F. Steeber, J. Abazi, and Susan Smith (University of Wisconsin-Madison) examined maternal-fetal iron interactions, since FASD outcomes are influenced by maternal iron status. Although it is well-known that alcohol exposure results in disruption of iron homeostasis in adults, little is known about the maternal-fetal interaction of iron homeostasis. A second trimester prenatal alcohol exposure model was used to examine fetal iron homeostasis. Findings suggested that PAE disrupted the ability of the fetal brain to correctly adapt to maternal iron status and these adaptive mechanisms were increasingly dysregulated under conditions of maternal iron deficiency. The authors concluded that further exploration is needed to understand the impact of maternal iron excess before options of maternal iron supplementation during pregnancy are pursued.

Kennedy Denys and Carmen Rasmussen (University of Alberta) reported on the use of a 23-item survey that assessed physical, emotional, social, school and cognitive domains relevant to the quality of life (QOL) of children with FASD as compared to those with just PAE and healthy controls, to explore the impact of this disability on overall wellbeing and adjustment. Both the FASD and PAE groups had lower scores on both child and parent ratings of school and cognitive functioning, and the FASD group had lower scores on parent rated emotional functioning. The findings suggested that impairments were seen in both the FASD and PAE groups despite the PAE groups not receiving a diagnosis or the associated supportive services that often accompany a diagnosis.

Vivian Lam, Wendy Comeau, C. Rainekei, W. Yu, L. Ellis, and Joanne Weinberg (The University of British Columbia) reported on the relationships between PAE and hypothalamic-pituitary-adrenal (HPA) reactivity. PAE appears to result in increased HPA tone and hyper-reactivity to stressors, including elevated corticosterone (CORT) and/or adrenocorticotropin (ACTH), throughout life. The investigators attempted to normalize HPA activity in an attempt to attenuate the impact of stressors after a history of PAE. Using a rat model of PAE, adult animals underwent a sham surgery or adrenalectomy with replacement of CORT at low basal levels (25 µg/ml in males and 75 µg/ml in females) and were then exposed to chronic mild stressors. Preliminary findings indicated a sexually dimorphic effect of prenatal treatment and/or chronic mild stressors on weight gain, modulation of PAE and/or stress induced anxiety-like behavior after normalizing CORT levels. Regulation of HPA activity may mediate the effect of PAE and chronic mild stressors on behavior.

Katarzyna Stepień¹, X. Zhang¹, S. Neumann¹, P. Pavlidis¹, G.G. Meadows², M. S. Kobor¹, and Joanne Weinberg¹ (University of British Columbia¹ and Washington State University²) explored the impact of PAE in long-term programming of neural gene expression related to neuroendocrine and neuroimmune functioning using an adjuvant-induced arthritis paradigm in a rat model. PAE was associated with an increased incidence, severity, and prolonged course of arthritis compared to ad libitum and pair-fed control animals. Gene expression was sampled in the prefrontal cortex and hippocampus. Among those with PAE, significant changes in gene expression were observed in both areas, including the *Acs13* gene, which has been shown to be methylated in response to environmental factors. PAE and pair-feeding resulted in altered responses to the adjuvant-induced arthritis. Although control animals demonstrated gene expression changes in response to the arthritis, animals with a history of PAE or pair-feeding had relatively few changes in gene expression. Further analysis of altered DNA methylation is needed to obtain potential epigenetic markers of PAE and to possibly index PAE-related changes in neuroendocrine and neuroimmune response.

FASt Data Presentations II: Neurodevelopmental Impact of Prenatal Alcohol Exposure

Maria Alejandra Infante, J. W. O'Brien, A. L. Ware, E. P. Riley, and Sarah Mattson (San Diego State University) studied the nature of specificity of attention deficits in children with

a history of PAE relative to non-exposed controls using neural activation of networks involved in attentional regulation. Adolescents who were matched on age, sex, handedness, ethnicity, and socioeconomic status were compared using the attention network test, which is a computerized task assessing the alerting, orienting, and executive control of attention. Although task performance did not differ by group status, children with a history of PAE demonstrated greater activation in all three brain network areas suggesting the attentional networks may be particularly sensitive to the effects of PAE.

Angelina Paolozza, D. P. Munoz, and James Reynolds (Queen's University) explored a new assessment tool for objectively quantifying the neurocognitive impact of PAE. A battery of saccadic eye movement tasks was used to assess deficits in executive function of children with FASD. Children with FASD made more timing errors, suggesting deficits in response inhibition, but did not make more sequence errors relative to control children. Children with FASD also exhibited significant deficits in saccade metrics, including accuracy and angle of trajectory, when compared to control children. In particular, the delayed memory saccade task appeared to effectively differentiate groups using indices of response inhibition and the integrity of sensory-motor circuits in the brain.

Ashley Ware¹, Benjamin Deweese¹, Elizabeth Sowell², Kenneth Lyon Jones³, Edward Riley¹, Sarah Mattson¹ and the CIFASD consortium (San Diego State University¹, University of Southern California², and University of California, San Diego³) studied the relationship between characteristics of the basal ganglia nuclei and executive functioning skills in children with and without PAE. Structural magnetic resonance imaging (MRI) and neurodevelopmental testing (subtests from the Delis-Kaplan Executive Function System) were completed on children between 8–16 years of age with and without a history of PAE. Reduced basal ganglia volume was associated with impaired executive functioning skills but the groups of children differed in the pattern of these relationships. Putamen volume accounted for executive functioning skills in exposed children and caudate volume accounted for these skills in non-exposed children, suggesting PAE results in altered neural circuitry. Using indices of regional brain volumes, logistic regression classification accuracy was 79.1%, indicating that structural brain anomalies may aid in the identification of children with FASD.

Catherine O'Leary¹, K.G. Thomas¹, C. D. Molteno¹, M. Kliegel¹, Joseph Jacobson², and Sandra Jacobson² (University of Cape Town¹ and Wayne State University²) reported on their work on prospective memory after a history of PAE. Although the impact of PAE on retrospective memory has been investigated in numerous studies, the impact on prospective memory, which is the ability to realize and act on delayed intentions, had not been previously explored. This study used a computerized car game to explore prospective memory differences in children classified as having FAS, partial FAS (pFAS), a history of heavy exposure without FAS/pFAS, and controls. PAE adversely impacted task performance, and performance on the more challenging non-focal prospective memory condition showed a significant difference after controlling for executive functioning, suggesting a distinct impairment in prospective memory skills.

FASt Data Presentations III: Biomarkers for Fetal Alcohol Spectrum Disorders

Dan Savage¹, M. J. Rosenberg¹, L. Coquet², M. W. Porch¹, C. Roux³, S. Jegou³, N. I. Perrone-Bizzozero¹, T. Joyenne², and B. J. Gonzalez³ (University of New Mexico School of Medicine¹, the Polymer, Biopolymer, Surfaces Laboratory, CNRG, UMR 6270, Proteomic Platform of the IFRMP23², and the University of Rouen³) explored gene expression changes in placenta that may serve as a biomarker for brain microvascular development. They reported that ethanol exposure in a rat model down-regulated expression of the gene, Placental Cerebral Cavernous Malformation Protein 3 (CCM-3) in both placenta and fetal

cerebral cortex. Reductions in this protein correlated with reductions in cerebral cortical microvascular development in regions like the ventricular and sub-ventricular zones, which are critical for normal brain development. Given CCM-3's role in brain vascular morphogenesis, the results of this study suggest that placental CCM-3 expression may serve as a biomarker for brain effects of prenatal ethanol exposure.

Conny Lin, Len Ke-Chih Huang, and Catherine Rankin (University of British Columbia) explored the molecular mechanisms underlying abnormalities in neurite outgrowth in a nematode (*C. elegans*) model for developmental alcohol exposure. They studied the effects of larval alcohol exposure on the stereotypic pattern of neurite outgrowth of two motor neurons, VC4 and VC5 that innervate the vulva and reported that in a majority of cases, larval alcohol exposure resulted in significant under-development of VC4 and VC5 neurites, though in a small group of animals, excessive neurite outgrowth was also observed. The presenter also reported on experiments where green fluorescent protein (GFP) was expressed downstream of the promoter for the nematode vesicular monoamine transporter, *cat-1*, and observed that larval ethanol exposure resulted in asymmetric gene expression. VC5 exhibited increased *cat-1* promoter activity, whereas VC4 exhibited decreased activity. These effects were not replicated by starvation suggesting that the effects of developmental alcohol exposure were not due to malnourishment. The stereotypic patterns of nematode motor neuron development and morphogenesis may facilitate the study of gene mutations that phenocopy the effects of developmental alcohol exposure.

Jay Ramadoss and Ronald Magness (University of Texas Medical Branch-Galveston) investigated alcohol-induced alterations in uterine angiogenesis-related mRNA abundance using tripartite digital mRNA technology on uterine arterial endothelial cells from third trimester ewes. Twenty genes were significantly down-regulated and two up-regulated. Using a tripartite digital gene expression system, the results indicated that alcohol has a negative effect on genes controlling uteroplacental angiogenesis and may alter key gestational adaptations required for fetal growth and developmental.

John Hannigan, L. M. Chiodo, V. Delaney-Black, R. J. Sokol, D. Ruden, A. Kruger, and S. Land (Wayne State University) identified a biomarker of PAE by looking at patterns of change in DNA methylation in human infant blood that was predictive of neurobehavioral deficits. From a larger prospective cohort of African American women, 5 at-risk PAE infants and 7 non-exposed infants provided infant heel-stick blood spots, which were analyzed using the Infinium Human Methylation 27 BeadChip. DNA methylation was then correlated to various outcome measures obtained at 4 years of age after controlling for maternal cigarette use. All 5 PAE infants had 9 to 15 hyper-methylated sites but 5 of the 7 controls had none and 2 of the controls had only 2 or 3. The degree of DNA hyper-methylation was related to memory, behavior, and fine motor problems at 4 years of age. Differential patterns of DNA methylation in human infant blood may detect children at risk based on their PAE and predict life-long neurobehavioral problems associated with FASD.

Nail Can Öztürk and Feng Zhou (Indiana University School of Medicine) explored expression of methyl CpG binding protein 2 (MeCP2) during cortical development after a history of PAE and contrasted that to ad lib or pair-fed mice. Mutations in MeCP2 have been linked to other neurodevelopmental disorders and it is known that it selectively binds to methylated DNA and is involved in transcriptional repression. PAE was associated with an increase in MeCP2.

Award Presentations

Annually, the FASDSG Merit award is presented to a junior research scientist whose record of scholarship indicates the likelihood for significant future success in the field of fetal alcohol research. Nathan Muraski of San Diego State University, a post-doctoral fellow of Jennifer Thomas, and a former graduate student of Mark Stanton of the University of Delaware, received the 2012 Merit Award. Dr. Muraski had 9 publications of which he was primary author on 4 and second author on 3. He was awarded the Oscar Kaplan Postdoctoral Fellowship in Developmental Issues and has received several conference travel awards, including one from the FASDSG in 2009. He presented a talk entitled “Neonatal alcohol exposure and the hippocampus: Insights from contextual fear conditioning in developing rats.” Dr. Muraski reviewed his multiple studies on the impact of developmental alcohol exposure on contextual and cued-learning, and linked the behavioral effects to changes in the hippocampus. He pointed out that neurobehavioral impairments and neuroanatomical aberrations have been found in humans with a history of PAE and animal models have indicated that timing, pattern, and level of alcohol exposure affect the severity of FASD. He noted that the hippocampus has been found to be especially vulnerable when alcohol exposure occurs during the brain growth spurt that typically occurs in the 3rd trimester in humans, which is equivalent to the 1st postnatal week in rodents. Dr. Murawski’s early work identified that contextual fear conditioning in rats is impaired in adulthood, after alcohol exposure on postnatal days 4–9. Using a paradigm to elicit the context pre-exposure facilitation effect (CPFE), he further explored the impact of alcohol delivered on postnatal days 4–9 (5.25g/kg/day) using this paradigm, which is known to be heavily dependent on the integrity of the hippocampus. The paradigm consists of pre-exposure to the stimulus on postnatal day (PD) 31, training on PD 32, and testing on PD 33. Postnatal days 4–9 alcohol exposure disrupted the CPFE and the impact of the exposure persisted into adulthood. In contrast, this exposure had no impact on cued-fear conditioning suggesting that the results were not due to overall performance effects. Additional studies suggested that CPFE impairment appeared to result from the action of alcohol on the developing hippocampus during the postnatal day 7–9 window. Furthermore, the CPFE impairment was found to be dose-dependent, with greater effects at higher blood alcohol concentrations. Reductions in CA1 c-Fos+ cells, pyramidal cells and behavior, including reductions in activity and impaired contextual fear conditioning, were seen in alcohol-exposed rats. He suggested that learning and memory impairment following developmental alcohol exposure may result from the impact of alcohol on the developing hippocampus as the timing and dose of alcohol exposure was related to the severity of hippocampal damage and degree of impairment on a behavioral task heavily dependent on hippocampal functioning.

Each year, the Henri Rosett award is presented to recognize the lifetime contributions of an individual to FASD prevention, treatment or research. The 2012 Henry Rosett award was presented to Dr. Denis Viljoen. Dr. Viljoen serves as chairperson and chief executive officer of the Foundation for Alcohol Related Research (FARR), Cape Town, South Africa. Over his lifetime of service, Dr Viljoen served in multiple leadership roles where he was in a position to influence and promote the diagnosis and treatment of FASD as a national priority. Among his many positions, Dr. Viljoen also served as Professor and Head of Department of Human Genetics, University of Witwatersrand, Johannesburg, as Deputy Chairman of the South African National Task Group for Genetic Services, and Advisor to South African Department of Health on Fetal Alcohol Syndrome. Dr. Viljoen’s nomination for the Rosett award received enthusiastic international support for the enormous effort that he spearheaded to identify the extent of FASD in South Africa and to bring international attention and resources to the diagnosis and treatment of children with fetal alcohol exposure. During his Rosett award acceptance speech, Dr. Viljoen spoke of the problems and challenges that came with identifying the enormous scope of alcoholism in general, and

fetal alcohol exposure in particular, in South Africa. He presented data on the role of readily available alcohol and lack of education on the incidence of alcoholism in South Africa. Dr. Viljeon described the relationship between poverty, alcoholism, malnutrition and diseases like tuberculosis and HIV/AIDS, a nexus of health challenges that he termed the “wheel of misfortune”. The consequences of alcoholism in South Africa included high rates of violence, mental illness and road accidents. Not surprisingly, as Dr. Viljeon was instrumental in discovering, the incidence of fetal alcohol exposure in South Africa is also extremely high, perhaps the highest in the world. For example, the prevalence of FAS in the towns of De Aar and Aurora was estimated as high as 12 to 13% of the population. The prevalence of FASD is expected to be significantly higher. Dr. Viljeon was instrumental in recruiting health care authorities in South Africa, researchers from the United States, as well as the National Institute on Alcohol Abuse and Alcoholism, to the task of diagnosing FASD in South Africa, under the aegis of FARR. In the second and third phases, FARR’s activities have focused on building community awareness of FASD and on prevention. To build community awareness and promote prevention, FARR reached out to health care providers, instituted a program titled “Healthy mother healthy baby”, and supported innovative ‘industrial theatre’ workshops. In towns like De Aar, FARR has instituted several programs including nutrition programs and stimulation, music and play therapy for FASD children. Dr. Viljeon provided an inspiring description of the long-term effort to build up community-based resources and support networks aimed at reducing alcohol use during pregnancy. Ongoing challenges (poverty, remote communities, ready access to alcohol) need to be addressed on a national scale in order to significantly reduce the incidence of FASD in South Africa. For heroic efforts in diagnosis, prevention and treatment of FASD in South Africa, FARR’s efforts under the leadership of Dr. Viljeon were recognized by the 2012 Henry Rosett Award.

Acknowledgments

Funding for this conference was made possible in part by funds from NIAAA and NICHD. The views expressed in written conference materials or publications, and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor imply endorsement by the U.S. Government.

References

- Fleisch AF, Wright RO, Baccarelli AA. Environmental epigenetics: a role in endocrine disease? *Journal of Molecular Endocrinology*. 2012; 49(2):R61–7. [PubMed: 22798698]
- Zizzo N, Di Pietro N, Green C, Reynolds J, Bell E, Racine E. Comments and Reflections on Ethics in Screening for Biomarkers of Prenatal Alcohol Exposure. *Alcoholism Clinical and Experimental Research*. 2013; 37(9):1451–1455.