June 2015 Issue 13

The International Medical e-Network devoted to

Fetal Alcohol Spectrum Disorders

NOFAS-UK
National Organisation for Fetal Alcohol Syndrome – UK
165 Beaufort Park,
London NW11 6DA, England
Helpline: 020 8458 5951
Email: info@nofas-uk.org
Website: www.nofas-uk.org
Charity No. 1101935
INTRODUCTION

The more we learn about FASD, the more we are able to create positive promising programmes and interventions to improve the lives of all those affected by Fetal Alcohol Spectrum Disorder.

When I adopted my daughter over 20 years ago, I had never heard of FAS or FASD. In 1999 when she was diagnosed with Fetal Alcohol Syndrome, not many doctors in the UK were aware of the condition. Though as far back as Greek times Aristotle noted, "Foolish, drunken and harebrained women most often bring forth children like unto themselves, morose and languid".

Now, since 1973 when Fetal Alcohol Syndrome was recognised and labelled in the United States by Drs Kenneth L. Jones and David W. Smith, research around the world has produced over two thousand FASD studies.

Every 6 months we publish abstracts of all new Fetal Alcohol research. In this issue of the FETAL ALCOHOL FORUM you will find abstracts of 168 studies, as well as original articles written for us by international FASD experts. Fetal Alcohol is beginning to get more recognition in the British media. (See articles from British newspapers: The Guardian and The Observer and listen to a radio interview).

Members of Parliament in the UK are taking action to improve health and awareness of FASD. On the 30th June MP Bill Esterson chaired the inaugural meeting of the All-Party Parliamentary Group (APPG) for FASD. This important initiative will put FASD higher on the UK Government agenda.

FASD researchers from around the world are collaborating and generating new international alliances. The European Fetal Alcohol Spectrum Disorder Alliance and the National Organization for Fetal Alcohol Syndrome Worldwide Network meet regularly on Skype.

There have been many new developments in the past year. New tools are helping to save research time and research budgets. New studies are delving deeper into alcohol’s effect on DNA and gene expression. New therapies are being developed for protection and even prevention of FASD. Though alcohol may cause premature birth, this is now being seen as one of nature’s ways of protecting the fetus from alcohol damage in the last trimester.

There is increasing evidence that we are beginning to conquer some of the challenges of FASD.
If you are reading this, you are part of our FASD GLOBAL FAMILY. You may live in one of the following countries that has produced new FASD studies in the past 6 months:

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>72</td>
</tr>
<tr>
<td>Canada</td>
<td>33</td>
</tr>
<tr>
<td>South Africa</td>
<td>9</td>
</tr>
<tr>
<td>Australia</td>
<td>5</td>
</tr>
<tr>
<td>UK</td>
<td>5</td>
</tr>
<tr>
<td>Argentina</td>
<td>4</td>
</tr>
<tr>
<td>Italy</td>
<td>4</td>
</tr>
<tr>
<td>China</td>
<td>4</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>4</td>
</tr>
<tr>
<td>Spain</td>
<td>4</td>
</tr>
<tr>
<td>UK</td>
<td>4</td>
</tr>
<tr>
<td>Germany</td>
<td>3</td>
</tr>
<tr>
<td>Iran</td>
<td>2</td>
</tr>
<tr>
<td>Japan</td>
<td>2</td>
</tr>
<tr>
<td>Netherlands</td>
<td>2</td>
</tr>
<tr>
<td>Sweden</td>
<td>2</td>
</tr>
<tr>
<td>Thailand</td>
<td>2</td>
</tr>
<tr>
<td>Brazil</td>
<td>1</td>
</tr>
<tr>
<td>Chile</td>
<td>1</td>
</tr>
<tr>
<td>Denmark</td>
<td>1</td>
</tr>
<tr>
<td>Finland</td>
<td>1</td>
</tr>
<tr>
<td>France</td>
<td>1</td>
</tr>
<tr>
<td>Israel</td>
<td>1</td>
</tr>
<tr>
<td>New Zealand</td>
<td>1</td>
</tr>
<tr>
<td>Poland</td>
<td>1</td>
</tr>
<tr>
<td>Russia</td>
<td>1</td>
</tr>
<tr>
<td>South Korea</td>
<td>1</td>
</tr>
<tr>
<td>Turkey</td>
<td>1</td>
</tr>
</tbody>
</table>

Total: 168

If you have an FASD study or news you would like us to publish in the next issue of the FETAL ALCOHOL FORUM, please send it to info@nofas-uk.org.

We always appreciate your comments and valuable feedback at info@nofas-uk.org. You can download issues of the FETAL ALCOHOL FORUM from our website: www.nofas-uk.org, or if you would like to be added to the FETAL ALCOHOL FORUM mailing list, please click here.

Susan Fleisher  
Publisher

Beata Ewertowska  
Editor/ Technical Supervisor

Elizabeth Mitchell  
Associate Editor
TABLE OF CONTENTS

*In the interest of brevity, Fetal Alcohol Spectrum Disorder has been abbreviated to FASD

- ORIGINAL ARTICLES BY FASD EXPERTS
- RESEARCH ABSTRACTS
- ARTICLE ABSTRACTS
- NEWS AND PRESS
I. **FASD in Denmark: What’s All the Fuss?**  
Janni Niclasen, PhD

II. **Assessing Children with FASD**  
Judith K. Eckerle Kang, MD

III. **Facing Fetal Alcohol Spectrum Disorder in Italy**  
Mauro Ceccanti, Daniela Fiorentino and Mario Vitalli

IV. **Rehabilitation for Children with Fetal Alcohol Spectrum Disorders (FASD) - A Unique Opportunity to Create a Holistic Forecast**  
Dr. Heike Hoff-Emden

V. **What Can We Learn from Cross-cultural Research on Alcohol Use in Pregnancy?**  
Lisa Schölin BSc, MSc, AFHEA

VI. **MicroRNA Biomarkers for the Effects of Fetal Alcohol Exposure**  
Rajesh C. Miranda, PhD.

VII. **Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE): An Area for Further Consideration**  
Jerrod Brown, Adam Piccolino, Judge Anthony Wartnik, Tina Andrews, Mary Weaver, Anne Russell, Hannah Brown, and Megan Lea
1. **Diagnosing FASD in Adults: The Development and Operation of an Adult FASD Clinic in Ontario, Canada**
   Valerie K. Temple, Jillian Ives, Ann Lindsay
   Publication – J Popul
   25th February 2015

   Jak Ozsarfati, Gideon Koren
   12th February 2015

3. **Investigating the Fetal and Postnatal Effects of Paternal Alcohol Exposure in Mouse Offspring: A Review**
   Marta Baber, Gideon Koren (Canada)
   22nd January, 2015

4. **Anticipatory Guidance for Children and Adolescents with Fetal Alcohol Spectrum Disorder (FASD): Practice Points for Primary Health Care Providers**
   Ana Hanlon-Dearman, Courtney R. Green, Gail Andrew, Nicole LeBlanc, Jocelynn L. Cook
   18th January, 2015

5. **The Cost of Lost Productivity Due to Fetal Alcohol Spectrum Disorder-Related Premature Mortality**
   Brian Easton, Larry Burd, Anna Sarnocinska-Hart, Jürgem Rehm, Svetlana Popova
   2nd January, 2015

   Susan J. Astley
   2nd January, 2015

7. **Associations between late and moderately preterm birth and smoking, alcohol, drug use and diet: a population-based case-cohort study**
   Smith LK, Draper ES, Evans TA, Field DJ, Johnson SJ, Manktelow BN, Seaton SE, Marlow N, Petrou S, Boyle EM (UK)

8. **Voluntary Exercise Partially Reverses Neonatal Alcohol-Induced Deficits in mPFC Layer II/III Dendritic Morphology of Male Adolescent Rats**
   Hamilton GF, Criss KJ, Klintsova AY (USA)
   29th October, 2014
   Back to Table of Contents

9. **Prevalence of Fetal Alcohol Syndrome in a South African City with a Predominantly Black African Population**
10. **Determination of direct alcohol markers: a review**
   Cabarcos P, Álvarez I, Tabernero MJ, Bermejo AM.; (Spain)
   Publication - Anal Bioanal Chem. [Epub ahead of print]
   3rd May 2015

11. **Computer-Delivered Screening and Brief Intervention for Alcohol Use in Pregnancy: A Pilot Randomized Trial.**
   22nd May 2015

12. **Reduction of Nfia gene expression and subsequent target genes by binge alcohol in the fetal brain**
   Mandal C, Park JH, Lee HT, Seo H, Chung IY, Choi IG, Jung KH, Chai YG. (Republic of Korea)
   15th October 2014

13. **Proceedings of the 2014 Annual Meeting of the Fetal Alcohol Spectrum Disorders Study Group**
   Reynolds JN, Valenzuela CF, Medina AE, Wozniak JR. (USA)
   23rd April 2015

14. **Placental Fatty Acid ethyl esters are elevated with maternal alcohol use in pregnancies complicated by prematurity**
   Gauthier TW, Mohan SS, Gross TS, Harris FL, Guidot DM, Brown LA. (USA)
   15th May 2015

15. **Effects of Ethanol on the Cerebellum: Advances and Prospects**
   Luo J. (USA)
   Publication - Cerebellum.
   2nd May 2015

16. **Editorial: Genetics and epigenetics of fetal alcohol spectrum disorders**
   Mason S, Zhou FC. (USA)
   Publication - Front Genet.;6:146. doi: 10.3389/fgene.2015.00146
   16th April 2015

[Back to Table of Contents]
17. **Hippocampal neuron populations are reduced in vervet monkeys with fetal alcohol exposure.**
   Burke MW, Ptito M, Ervin FR, Palmour RM. (USA)
   May 2015

18. **Sonographic findings in an isolated widened fetal subarachnoid space**
   Tongsong T, Puntachai P, Tongprasert F, Srisupundit K, Luewan S, Traisrisilp K. (Thailand)
   May 2015

19. **Alcohol consumption during pregnancy and adverse neurodevelopmental outcomes**
   Vall O, Salat-Batlle J, Garcia-Algar O (Spain)
   Publication - J Epidemiol Community Health doi:10.1136/jech-2014-203938

20. **Developmental exposure to ethanol increases the neuronal vulnerability to oxygen-glucose deprivation in cerebellar granule cell cultures**
   Le Duc D, Spataru A, Ceanga M, Zagrean L, Schöneberg T, Toescu EC, Zagrean AM (Germany, Romania, UK)
   Publication - Brain Res. pii: S0006-8993(15)00298-X. doi: 10.1016
   13th April 2015

21. **Fetal programming and cardiovascular pathology**
   Alexander BT, Dasinger JH, Intapad S. (USA)
   1st May 2015

22. **Sustained action of developmental ethanol exposure on the cortisol response to stress in zebrafish larvae and adults.**
   Baiamonte M, Brennan CH, Vinson GP. (UK)
   13th April 2015

23. **Frequency and epidemiologic aspects of male infertility.**
   Sohravand F, Jafari M, Shariat M, Haghollahi F, Lotfi M (Iran)
   April 2015

[Back to Table of Contents]
24. **Postnatal ethanol exposure alters levels of 2-arachidonylglycerol-metabolizing enzymes and pharmacological inhibition of monoacylglycerol lipase does not cause neurodegeneration in neonatal mice.**
   Subbanna S, Psychoyos D, Xie S, Basavarajappa BS. (USA)
   10th April 2015

25. **Transient activation of microglia following acute alcohol exposure in developing mouse neocortex is primarily driven by BAX-dependent neurodegeneration.**
   Ahlers KE, Karaçay B, Fuller L, Bonthius DJ, Dailey ME. (USA)
   9th April 2015

26. **Fetal alcohol spectrum disorders in Australia - the future is prevention.**
   Elliott EJ.; elizabeth.elliott@health.nsw.gov.au (Australia)
   30th March 2015

27. **Cost attributable to Fetal Alcohol Spectrum Disorder in the Canadian correctional system.**
   Popova S, Lange S, Burd L, Rehm J
   Publication - Int J Law Psychiatry. pii: S0160-2527(15)00049-7. doi: 10.1016/j.ijlp.2015.03.010
   3rd April 2015

28. **Neural correlates of cerebellar-mediated timing during finger tapping in children with fetal alcohol spectrum disorders.**
   du Plessis L, Jacobson SW, Molteno CD, Robertson FC, Peterson BS, Jacobson JL, Meintjes EM.
   (South Africa, USA)
   24th December 2014

29. **The Association of Prenatal Exposure to Perfluorinated Chemicals with Maternal Essential and Long-Chain Polyunsaturated Fatty Acids during Pregnancy and the Birth Weight of their Offspring: The Hokkaido Study.**
   Publication - Environ Health Perspect.
   3rd April 2015

30. **The effects of postnatal alcohol exposure and galantamine on the context pre-exposure facilitation effect and acetylcholine efflux using in vivo microdialysis.**
   Perkins AE, Fadel JR, Kelly SJ.; address: sandra-kelly@sc.edu (USA)
   May 2015
31. **Verbal learning and memory impairment in children with fetal alcohol spectrum disorders.**
Lewis CE, Thomas KG, Dodge NC, Molteno CD, Meintjes EM, Jacobson JL, Jacobson SW. (South Africa)

32. **Eye movements reveal sexually dimorphic deficits in children with fetal alcohol spectrum disorder.**
Paolozza A, Munn R, Munoz DP, Reynolds JN. (Canada)

33. **Reduced DNA methylation at the PEG3 DMR and KvDMR1 loci in children exposed to alcohol in utero: a South African Fetal Alcohol Syndrome cohort study.**
Masemola ML, van der Merwe L, Lombard Z, Viljoen D, Ramsay M. (South Africa)

34. **The protective effect of vitamin E against prenatal and early postnatal ethanol treatment-induced heart abnormality in rats: A 3-month follow-up study.**
Shirpoor A, Nemati S, Ansari MH, Ilkhanizadeh B. (Iran)

35. **Using a single binge drinking question to identify Russian women at risk for an alcohol-exposed pregnancy.**
Balachova T, Sobell LC, Agrawal S, Isurina G, Tsvetkova L, Volkova E, Bohora S

36. **Alcohol-induced histone H3K9 hyperacetylation and cardiac hypertrophy are reversed by a histone acetylases inhibitor anacardic acid in developing murine hearts.**

37. **Postnatal administration of allopregnanolone modifies glutamate release but not BDNF content in striatum samples of rats prenatally exposed to ethanol.**
Yunes R, Estrella CR, Garcia S, Lara HE, Cabrera R. (Argentina, Chile)

Back to Table of Contents
38. **Message on a bottle.**
Burton A. (Australia)
April 2015

39. **Self-regulation therapy increases frontal gray matter in children with fetal alcohol spectrum disorder: evaluation by voxel-based morphometry.**
Soh DW, Skocic J, Nash K, Stevens S, Turner GR, Rovet J. (Canada)
Publication - Front Hum Neurosci. 9:108. doi: 10.3389/fnhum.2015.00108
4th March 2015

40. **The Medical Symptom Validity Test Measures Effort Not Ability in Children: A Comparison Between Mild TBI and Fetal Alcohol Spectrum Disorder Samples.**
Gidley Larson JC, Flaro L, Peterson RL, Connery AK, Baker DA, Kirkwood MW
May 2015

41. **White matter integrity of the cerebellar peduncles as a mediator of effects of prenatal alcohol exposure on eyblinking conditioning.**
Fan J, Meintjes EM, Molteno CD, Spottiswoode BS, Dodge NC, Alhamud AA, Stanton ME, Peterson BS, Jacobson JL, Jacobson SW. (South Africa)
17th March 2015

42. **Neuroimaging effects of prenatal alcohol exposure on the developing human brain: a magnetic resonance imaging review.**
Donald KA, Eastman E, Howells FM, Adnams C, Riley EP, Woods RP, Narr KL, Stein DJ (USA, South Africa)

43. **Do pediatricians recognize fetal alcohol spectrum disorders in children with developmental and behavioral problems?**
Rojmahamongkol P, Cheema-Hasan A, Weitzman C (Thailand)
April 2015

44. **Methods for surveillance of fetal alcohol syndrome: The Fetal Alcohol Syndrome Surveillance Network II (FASSNetII) - Arizona, Colorado, New York, 2009 - 2014.**
March 2015
Back to Table of Contents
Kreitinger C, Gutierrez H, Hamidovic A, Schmitt C, Sarangarm P, Rayburn WF, Leeman L, Bakhireva LN. (USA)
Publication - J Matern Fetal Neonatal Med. 23:1-6
March 2015

46. Visual search for feature conjunctions: an fMRI study comparing alcohol-related neurodevelopmental disorder (ARND) to ADHD.
O’Conaill CR, Malisza KL, Buss JL, Bolster RB, Clancy C, de Gervai PD, Chudley AE, Longstaffe S. (Canada)
4th March 2015

47. Alcohol use disorders in pregnancy.
DeVido J, Bogunovic O, Weiss RD. (USA)
March-April 2015

48. Docosahexaenoic acid partially ameliorates deficits in social behavior and ultrasonic vocalizations caused by prenatal ethanol exposure.
Wellmann KA, George F, Brnouti F, Mooney SM. (USA)
Publication - Behav Brain Res. 286:201-11. doi: 10.1016/j.bbr.2015.02.048
1st June 2015

49. Dose effect of gestational ethanol exposure on placentation and fetal growth.
Gundogan F, Gilligan J, Qi W, Chen E, Naram R, de la Monte SM. (USA)
Publication - Placenta. 36(5):523-30. doi: 10.1016/j.placenta.2015.02.010
May 2015

50. Executive function and cortical thickness in youths prenatally exposed to cocaine, alcohol and tobacco
Gautam P, Warner TD, Kan EC, Sowell ER. (USA)
2nd February 2015

51. Maternal L-glutamine supplementation prevents prenatal alcohol exposure-induced fetal growth restriction in an ovine model.
Sawant OB, Wu G, Washburn SE. (USA)
June 2015

Back to Table of Contents
52. **Diagnosing FASD in adults: the development and operation of an adult FASD clinic in Ontario, Canada.**

Temple VK, Ives J, Lindsay A. (Canada)

53. **Maternal alcohol intake around the time of conception causes glucose intolerance and insulin insensitivity in rat offspring, which is exacerbated by a postnatal high-fat diet.**

Gårdebjer EM, Anderson ST, Pantalone M, Wlodek ME, Moritz KM. (Australia)
2nd March 2015

54. **A South African mixed race lip/philtrum guide for diagnosis of fetal alcohol spectrum disorders.**

April 2015

55. **Volume changes and brain-behavior relationships in white matter and subcortical gray matter in children with prenatal alcohol exposure.**

June 2015

56. **Hypothalamic-pituitary-adrenal axis and behavioral dysfunction following early binge-like prenatal alcoholexposure in mice.**

Wieczorek L, Fish EW, O'Leary-Moore SK, Parnell SE, Sulik KK. (USA)
Publication - Alcohol. 49(3):207-17. doi: 10.1016/j.alcohol.2015.01.005
May 2015

57. **Alcohol odor elicits appetitive facial expressions in human neonates prenatally exposed to the drug.**

Faas AE, March SM, Moya PR, Molina JC. (Argentina)
Publication - Physiol Behav. pii: S0031-9384(15)00105-5. doi: 10.1016/j.physbeh.2015.02.031
21st February 2015

58. **Emotion recognition in children with Fetal Alcohol Spectrum Disorders.**

Kerns KA, Siklos S, Baker L, Müller U. (Canada)
Publication - Child Neuropsychol. 1-21.
23rd February 2015

Back to Table of Contents
59. **Fatty acid ethyl esters disrupt neonatal alveolar macrophage mitochondria and derange cellular functioning.**
Mohan SS, Ping XD, Harris FL, Ronda NJ, Brown LA, Gauthier TW. (USA)
March 2015

60. **Acetaldehyde, not ethanol, impairs myelin formation and viability in primary mouse oligodendrocytes.**
Coutts DJ, Harrison NL. (USA)
March 2015

61. **Pioglitazone blocks ethanol induction of microglial activation and immune responses in the hippocampus, cerebellum, and cerebral cortex in a mouse model of fetal alcohol spectrum disorders.**
Drew PD, Johnson JW, Douglas JC, Phelan KD, Kane CJ. (USA)
19 February 2015

62. **Transcriptomic study of mouse embryonic neural stem cell differentiation under ethanol treatment.**
Mandal C, Park JH, Choi MR, Kim SH, Badejo AC, Chai JC, Lee YS, Jung KH, Chai YG. (Republic of Korea)
20th February 2015

63. **Cognitive and executive functions, social cognition and sense of coherence in adults with fetal alcohol syndrome.**
Rangmar J, Sandberg AD, Aronson M, Fahlke C. (Sweden)
Publication - Nord J Psychiatry.
20th February 2015

64. **Prevalence and patterns of alcohol use in pregnancy in remote Western Australian communities: The Liliwan Project.**
Fitzpatrick JP, Latimer J, Ferreira ML, Carter M, Oscar J, Martiniuk AL, Watkins RE, Elliott EJ. (Australia)
19th February 2015

Back to Table of Contents
65. **Lifestyle, pregnancy and epigenetic effects.**
Barua S1, Junaid MA. (USA)
February 2015

66. **Genetic absence of nNOS worsens fetal alcohol effects in mice. I: behavioral deficits.**
Karacay B, Bonthius NE, Plume J, Bonthius DJ. (USA)
February 2015

67. **The neuronal nitric oxide synthase (nNOS) gene and neuroprotection against alcohol toxicity.**
Karacağ B, Bonthius DJ. (USA)
May 2015

68. **[Alcohol and pregnancy: advantage of a screening questionnaire -- a population study].**
Lherault S, Chauleur C. (France) [Article in French]
December 2014

69. **Effect of boric acid on oxidative stress in rats with fetal alcohol syndrome.**
Sogut I, Oglakci A, Kartkaya K, Ol KK, Sogut MS, Kanbak G, Inal ME. (Turkey)
March 2015

70. **Genetic absence of nNOS worsens fetal alcohol effects in mice. II: microencephaly and neuronal losses.**
Karacay B, Mahoney J, Plume J, Bonthius DJ. (USA)
9th February 2015

71. **Endogenous opioids as substrates for ethanol intake in the neonatal rat: The impact of prenatal ethanol exposure on the opioid family in the early postnatal period.**
Bordner K, Deak T. (USA)
7th February 2015
72. **Screening for fetal alcohol spectrum disorders by nonmedical community workers.**
   O'Connor MJ, Rotheram-Borus MJ, Tomlinson M, Bill C, LeRoux IM, Stewart J. (South Africa)
   18th November 2014

73. **A study of the effects of prenatal alcohol exposure on white matter microstructural integrity at birth.**
   Donald KA, Roos A, Fouche JP, Koen N, Howells FM, Woods RP, Zar HJ, Narr KL, Stein DJ. (South Africa)
   Publication - Acta Neuropsychiatr.
   29th May 2015

74. **"If you can have one glass of wine now and then, why are you denying that to a woman with no evidence": Knowledge and practices of health professionals concerning alcohol consumption during pregnancy.**
   Crawford-Williams F, Steen M, Esterman A, Fielder A, Mikocka-Walus A. (Australia)
   4th May 2015

75. **"My midwife said that having a glass of red wine was actually better for the baby": a focus group study of women and their partner's knowledge and experiences relating to alcohol consumption in pregnancy.**
   Crawford-Williams F, Steen M, Esterman A, Fielder A, Mikocka-Walus A. (Australia, UK)
   1st April 2015

76. **Children adopted from Poland display a high risk of foetal alcohol spectrum disorders and some may go undiagnosed.**
   Knuiman S, Rijk CH, Hoksbergen RA, van Baar AL. (The Netherlands)
   February 2015

77. **What does the general public in the UK know about the risk to a developing foetus if exposed to alcohol in pregnancy? Findings from a UK mixed methodology study.**
   Mukherjee R, Wray E, Hollins S, Curfs L. (UK)
   May 2015

78. **Effects of all three trimester moderate binge alcohol exposure on the foetal hippocampal formation and olfactory bulb.**
   Washburn SE, Ramadoss J, Chen WJ, Cudd TA. (USA)
   2nd September 2014

*Back to Table of Contents*
79. **Prenatal ethanol exposure and placental hCG and IGF2 expression.**
   19th May 2015

80. **Prenatal factors associated with Autism Spectrum Disorder (ASD).**
   Ornoy A, Weinstein-Fudim L, Ergaz Z. (Israel)
   Publication - Reprod Toxicol.: S0890-6238(15)00075-1. doi: 10.1016/j.reprotox.2015.05.007.
   25th May 2015

81. **Nicotine and ethanol co-use in Long-Evans rats: Stimulatory effects of perinatal exposure to a fat-rich diet.**
   Karatayev O, Lukatskaya O, Moon SH, Guo WR, Chen D, Algava D, Abedi S, Leibowitz SF. (USA)
   11th April 2015

82. **Early maternal alcohol consumption alters hippocampal DNA methylation, gene expression and volume in a mouse model.**
   Marjonen H, Sierra A, Nyman A, Rogojin V, Gröhn O, Linden AM, Hautaniemi S, Kaminen-Ahola N. (Finland)
   13th May 2015

83. **Paternal alcohol exposure in mice alters brain NGF and BDNF and increases ethanol-elicited preference in male offspring.**
   4th May 2015

84. **Ethanol exposure induces neonatal neurodegeneration by enhancing CB1R Exon1 histone H4K8 acetylation and up-regulating CB1R function causing neurobehavioral abnormalities in adult mice.**
   Subbanna S, Nagre NN, Umapathy NS, Pace BS, Basavarajappa BS. (USA)
   31st October 2015

85. **Prenatal ethanol exposure impairs executive function in mice into adulthood.**
   Marquardt K, Sigdel R, Caldwell K, Brigman JL. (USA)
   December 2014

Back to Table of Contents
Popoola DO, Borrow AP, Sanders JE, Nizhnikov ME, Cameron NM. (USA)
Publication - Physiol Behav.: S0031-9384(15)00003-7. doi: 10.1016/j.physbeh.2015.01.001.
7th January 2015

87. [Potential therapy of intravenous neural stem cell transplantation for psychiatric disorder—a strategy for facilitation of neural network and behavioral recovery].
Shirasaka T, Kurosawa S. (Japan) [Article in Japanese]
October 2014

88. Embryo transfers between C57BL/6J and DBA/2J mice: Examination of a maternal effect on ethanol teratogenesis.
Gilliam D. (USA)
1th December 2014

89. CB1-receptor knockout neonatal mice are protected against ethanol-induced impairments of DNMT1, DNMT3A, and DNA methylation.
Nagre NN, Subbanna S, Shivakumar M, Psychoyos D, Basavarajappa BS. (USA)
February 2015

90. Fetal alcohol exposure increases susceptibility to carcinogenesis and promotes tumor progression in prostate gland.
Sarkar DK. (USA)

91. Choline partially prevents the impact of ethanol on the lipid raft dependent functions of l1 cell adhesion molecule.
Tang N, Bamford P, Jones J, He M, Kane MA, Mooney SM, Bearer CF. (USA)
November 2014

92. Zinc insufficiency mediates ethanol-induced alveolar macrophage dysfunction in the pregnant female mouse.
Konomi JV, Harris FL, Ping XD, Gauthier TW, Brown LA. (USA)
January 2015

Back to Table of Contents
93. Executive Functioning in Children and Adolescents Prenatally Exposed to Alcohol: A Meta-Analytic Review.
Khoury JE, Milligan K, Girard TA. (Canada)
Publication- Neuropsychol Rev.
3rd June 2015

94. Anterior Cingulate Cortex Surface Area Relates to Behavioral Inhibition in Adolescents with and without Heavy Prenatal Alcohol Exposure.
Migliorini R, Moore EM, Glass L, Infante MA, Tapert SF, Jones KL, Mattson SN, Riley EP. (USA)
Publication - Behav Brain Res.: S0166-4328(15)30002-4. doi: 10.1016/j.bbr.2015.05.037.
26th May 2015

95. MiR-125b protects against ethanol-induced apoptosis in neural crest cells and mouse embryos by targeting Bak 1 and PUMA.
Chen X, Liu J, Feng WK, Wu X, Chen SY. (USA)
27th May 2015

96. Preventing alcohol-exposed pregnancy among an American Indian/Alaska Native population: effect of a screening, brief intervention, and referral to treatment intervention.
Montag AC, Brodine SK, Alcaraz JE, Clapp JD, Allison MA, Calac DJ, Hull AD, Gorman JR, Jones KL, Chambers CD. (USA)
January 2015

97. Ethanol deregulates Mecp2/MeCP2 in differentiating neural stem cells via interplay between 5-methylcytosine and 5-hydroxymethylcytosine at the Mecp2 regulatory elements.
Liyanage VR, Zachariah RM, Davie JR, Rastegar M. (Canada)
March 2015

98. Ethanol exposure induces a delay in the reacquisition of function during head regeneration in Schmidtea mediterranea.
Lowe JR, Mahool TD, Staehle MM. (USA)
19th January 2015

99. Experimental Models of Early Exposure to Alcohol: A Way to Unravel the Neurobiology of Mental Retardation
Alberto Granato, Andrea De Giorgio, (Italy)
6th January 2015
100. **Community translation of the Math Interactive Learning Experience Program for children with FASD.**
Kable JA, Taddeo E, Strickland D, Coles CD. (USA)
16th January 2015

101. **Misdiagnosis and missed diagnoses in foster and adopted children with prenatal alcohol exposure.**
Chasnoff IJ, Wells AM, King L. (USA)
12 January 2015

102. **Salivary cortisol levels are elevated in the afternoon and at bedtime in children with prenatal alcohol exposure.**
Keiver K, Bertram CP, Orr AP, Clarren S. (Canada)
February 2015

103. **Epigenetics in pediatrics.**
Puumala SE, Hoyme HE. (USA)
January 2015

104. **Embryonic alcohol exposure impairs the dopaminergic system and social behavioral responses in adult zebrafish.**
Fernandes Y, Rampersad M, Gerlai R. (Canada)
7th January 2015

105. **Moderate prenatal alcohol exposure and quantification of social behavior in adult rats.**
Hamilton DA, Magcalas CM, Barto D, Bird CW, Rodriguez CI, Fink BC, Pellis SM, Davies S, Savage DD. (USA)
14th December 2014

106. **Psychosocial outcomes of fetal alcohol syndrome in adulthood.**
January 2015

[Back to Table of Contents]
107. **Comparisons of Intelligence and Behavior in Children With Fetal Alcohol Spectrum Disorder and ADHD.**
Raldiris TL, Bowers TG, Towsey C. (USA)
Publication - J Atten Disord.: 1087054714563792.
18th December 2014

108. **The effects of prenatal exposure to alcohol and environmental tobacco smoke on risk for ADHD: a large population-based study.**
Han JY, Kwon HJ, Ha M, Paik KC, Lim MH, Gyu Lee S, Yoo SJ, Kim EJ. (South Korea)
30th January 2015

109. **A deficit in face-voice integration in developing vervet monkeys exposed to ethanol during gestation.**
Zangenehpour S, Javadi P, Ervin FR, Palmour RM, Ptito M. (Canada, Denmark)
3rd December 2014

110. **Maternal risk factors for fetal alcohol spectrum disorders in a province in Italy.**
1st December 2014

111. **Effect of repeated alcohol exposure during the third trimester-equivalent on messenger RNA levels for interleukin-1β, chemokine (C-C motif) ligand 2, and interleukin 10 in the developing rat brain after injection of lipopolysaccharide.**
Topper LA, Valenzuela CF. (USA)
December 2014

112. **Deficient PKR in RAX/PKR Association Ameliorates Ethanol-Induced Neurotoxicity in the Developing Cerebellum.**
Li H, Chen J, Qi Y, Dai L, Zhang M, Frank JA, Handshoe JW, Cui J, Xu W, Chen G. (USA)
Publication - Cerebellum.
16th January 2015

113. **PCDH14- and GABRB1-like nervous system developmental genes are altered during early neuronal differentiation of NCCIT cells treated with ethanol.**
Halder D, Mandal C, Lee B, Lee J, Choi M, Chai J, Lee Y, Jung K, Chai Y. (Republic of Korea)
Publication - Hum Exp Toxicol.: 0960327114566827.
6th January 2015

**Back to Table of Contents**
114. **Familiäre Belastungen in Pflege- und Adoptionsfamilien mit Kindern mit fetalem Alkoholsyndrom.** [Article in German]
Sarimski K.

115. **Effect of lipid raft disruption on ethanol inhibition of L1 adhesion.**
Dou X, Charness ME. (USA)

116. **Amphetamine sensitization and cross-sensitization with acute restraint stress: impact of prenatal alcohol exposure in male and female rats.**
Uban KA, Comeau WL, Bodnar T, Yu WK, Weinberg J, Galea LA. (Canada)

117. **Evaluation of a Multilevel and Integrated Program to Raise Awareness of the Harmful Effects of Prenatal Alcohol Exposure in a Local Community**
Publication - Alcohol Alcohol. pii: agv051. 27th May 2015

118. **Effects of developmental alcohol exposure vs. intubation stress on BDNF and TrkB expression in the hippocampus and frontal cortex of neonatal rats.**
Boschen KE, Criss KJ, Palamarchouk V, Roth TL, Klintsova AY. (USA)

119. **Prenatal alcohol exposure and adolescent stress increase sensitivity to stress and gonadal hormone influences on cognition in adult female rats.**
Comeau WL, Lee K, Anderson K, Weinberg J. (Canada)

120. **Dissecting FASD through the global transcriptome.**
Zhou FC. (USA)

121. **Pharmacological treatment of disruptive behavior in children with fetal alcohol spectrum disorder.**
Koren G. (Canada)

Back to Table of Contents
122. Apoptotic cell death and temporal expression of apoptotic proteins Bcl-2 and Bax in the hippocampus, following binge ethanol in the neonatal rat model.
Smith CC, Guévremont D, Williams JM, Napper RM. (New Zealand)
January 2015

123. Ethanol exposure during gastrulation alters neuronal morphology and behavior in zebrafish.
Shan SD, Boutin S, Ferdous J, Ali DW. (Canada)
16th January 2015

124. Looking further upstream to prevent fetal alcohol spectrum disorder in Canada.
Sanders J, Currie CL. (Canada)

125. Zebrafish retinal defects induced by ethanol exposure are rescued by retinoic acid and folic acid supplement.
Muralidharan P, Sarmah S, Marrs JA. (USA)
March 2015

126. Gypenosides protected the neural stem cells in the subventricular zone of neonatal rats that were prenatally exposed to ethanol.
Dong L, Yang KQ, Fu WY, Shang ZH, Zhang QY, Jing FM, Li LL, Xin H, Wang XJ. (China)
28th November 2014

127. Pre- and postnatal exposure to moderate levels of ethanol can have long-lasting effects on hippocampal glutamate uptake in adolescent offspring.
Brolese G, Lunardi P, de Souza DF, Lopes FM, Leite MC, Gonçalves CA. (Brazil)
15th May 2015

128. Correlates of partner support to abstain from prenatal alcohol use: a cross-sectional survey among Dutch partners of pregnant women.
van der Wulp NY, Hoving C, de Vries H. (The Netherlands)
5th May 2015

Back to Table of Contents
129. [Effect of prenatal alcohol exposure on rhythmic respiratory discharge activity in medullary slices of neonatal rats]. [Article in Chinese]
Ji ML, Qian ZB, Wu YH. (China)
April 2015

130. Alcohol and pregnancy: Effects on maternal care, HPA axis function, and hippocampal neurogenesis in adult females.
Workman JL, Raineki C, Weinberg J, Galea LA. (Canada)
9th March 2015

131. In Utero exposure to low-dose alcohol induces reprogramming of mammary development and tumor risk in MMTV-erbB-2 transgenic mice.
Ma Z, Blackwelder AJ, Lee H, Zhao M, Yang X. (USA)
7th April 2015

132. Prenatal ethanol increases ethanol intake throughout adolescence, alters ethanol-mediated aversive learning, and affects μ but not δ or κ opioid receptor mRNA expression.
Fabio MC, Macchione AF, Nizhnikov ME, Pautassi RM. (Argentina)
9th April 2015

133. Effects of ethanol exposure in utero on Cajal-Retzius cells in the developing cortex.
Skorput AG, Yeh HH. (Lebanon, USA)
May 2015

134. The impact of prenatal alcohol exposure on hippocampal-dependent outcome measures is influenced by prenataland early-life rearing conditions.
Caldwell KK, Goggin SL, Labrecque MT, Allan AM. (USA)
April 2015

135. Moderate prenatal alcohol exposure enhances GluN2B containing NMDA receptor binding and ifenprodil sensitivity in rat agranular insular cortex.
Bird CW, Candelaria-Cook FT, Magcalas CM, Davies S, Valenzuela CF, Savage DD, Hamilton DA. (USA)
6th March 2015

Back to Table of Contents
136. **Prenatal alcohol exposure alters steady-state and activated gene expression in the adult rat brain.**
Lussier AA, Stepien KA, Neumann SM, Pavlidis P, Kobor MS, Weinberg J. (Canada)
February 2015

137. **Cognitive Factors Contributing to Spelling Performance in Children With Prenatal Alcohol Exposure.**
Glass L, Graham DM, Akshoomoff N, Mattson SN.
Publication - Neuropsychology.
2nd February 2015

138. **β-endorphin neuronal transplantation into the hypothalamus alters anxiety-like behaviors in prenatal alcohol-exposed rats and alcohol-non-prefering and alcohol-prefering rats.**
January 2015

139. **Clinical sensitivity and specificity of meconium fatty acid ethyl ester, ethyl glucuronide, and ethyl sulfate for detecting maternal drinking during pregnancy.**
March 2015

140. **Effects of prenatal alcohol and cigarette exposure on offspring substance use in multiplex, alcohol-dependent families.**
O'Brien JW, Hill SY. (USA)
December 2014

141. **Moderate-level prenatal alcohol exposure induces sex differences in dopamine d1 receptor binding in adult rhesus monkeys.**
Converse AK, Moore CF, Holden JE, Ahlers EO, Moirano JM, Larson JA, Resch LM, DeJesus OT, Barnhart TE, Nickles RJ, Murali D, Christian BT, Schneider ML. (USA)
December 2014

142. **Using optical coherence tomography to rapidly phenotype and quantify congenital heart defects associated with prenatal alcohol exposure.**
Karanamuni G, Gu S, Doughman YQ, Noonan AI, Rollins AM, Jenkins MW, Watanabe M. (USA)
April 2015

Back to Table of Contents
143. **Importance of genetics in fetal alcohol effects: null mutation of the nNOS gene worsens alcohol-induced cerebellar neuronal losses and behavioral deficits.**
Bonthius DJ Jr, Winters Z, Karacay B, Bousquet SL, Bonthius DJ. (USA)
January 2015

144. **Effects of low-level alcohol use on cognitive interference: an fMRI study in young adults.**
Hatchard T, Smith AM, Halchuk RE, Longo CA, Fried PA, Hogan MJ, Cameron I. (Canada)
February 2015

145. **Low-to-moderate prenatal alcohol consumption and the risk of selected birth outcomes: a prospective cohort study.**
Lundsberg LS, Illuzzi JL, Belanger K, Triche EW, Bracken MB. (USA)
January 2015

146. **Neonatal sensitization to ethanol-induced breathing disruptions as a function of late prenatal exposure to the drug in the rat: modulatory effects of ethanol’s chemosensory cues.**
Cullere M, Macchione AF, Haymal B, Paradelo M, Langer MD, Spear NE, Molina JC. (Argentina)
February 2015

147. **Mental and Motor Development of Children with Preterm Birth and Children with Fetal Alcohol Syndrome.**
Feldmann R, Girke N. (Germany)
Publication - Klin Padiatr.
3rd June 2015

148. **Reversal of glucose intolerance in rat offspring exposed to ethanol before birth through reduction of nuclear skeletal muscle HDAC expression by the bile acid TUDCA.**
Yao XH, Nguyen KH, Nyomba BL. (Canada)
23rd December 2014

149. **Prenatal alcohol exposure alters response of kisspeptin-ir neurons to estradiol and progesterone in adult female rats.**
Sliwowska JH1, Bodnar TS, Weinberg J. (Poland)
November 2014

[Back to Table of Contents]
150. Maternal Alcohol Consumption before and during Pregnancy and the Risks of Congenital Heart Defects in Offspring: A Systematic Review and Meta-analysis.
Sun J, Chen X, Chen H, Ma Z, Zhou J. (China)
1st June 2015

151. FAS, FASD: Diagnosis and Myths.
Barry C. Stanley (Canada)
23rd March 2015

152. Implementing staff-administered TACER-3 alcohol screening in an antenatal clinic.
Lisa Chiodo, John Hannigan, Shobha Mehta, James Janisse, Virginia Delaney-Black, Deborah Walker, Robert Sokol
Publication - AJOG Volume 212, Issue 1, Supplement, Pages S106–S107
January 2015

153. Prenatal ethanol exposure alters ethanol-induced Fos immunoreactivity and dopaminergic activity in the mesocorticolimbic pathway of the adolescent brain.
Fabio MC, Vivas L, Pautassi RM. (Argentina)
6th June 2015

154. Impaired arousal in rat pups with prenatal alcohol exposure is modulated by GABAergic mechanisms.
Sirieix CM, Tobia CM, Schneider RW, Darnall RA. (USA)
June 2015

155. Ethanol-related alterations in gene expression patterns in the developing murine hippocampus.
Mandal C, Park KS, Jung KH, Chai YG. (Republic of Korea)
Publication - Acta Biochim Biophys Sin (Shanghai). pii: gmv050.
10th June 2015

156. Costs of Fetal Alcohol Spectrum Disorder in the Canadian Criminal Justice System.
Thanh NX, Jonsson E. (Canada)
1st June 2015

Back to Table of Contents
157. **Effect of Depression on Risky Drinking and Response to a Screening, Brief Intervention, and Referral to Treatment Intervention.**
Montag AC, Brodine SK, Alcaraz JE, Clapp JD, Allison MA, Calac DJ, Hull AD, Gorman JR, Jones KL, Chambers CD. (USA)
11th June 2015

158. **Exposure to tobacco, alcohol and drugs of abuse during pregnancy. A study of prevalence among pregnant women in Malaga (Spain).**
17th June 2015

159. **Alcohol use, smoking and their co-occurrence during pregnancy among Canadian women, 2003 to 2011/12.**
Lange S, Probst C, Quere M, Rehm J, Popova S. (Canada, France, Germany)
14th June 2015

160. **The Knowledge of Rehabilitation Professionals Concerning Fetal Alcohol Spectrum Disorders.**
Birch SM, Carpenter HA, Marsh AM, McClung KA, Doll JD. (USA)

161. **Virtual Sensorimotor Balance Training for Children With Fetal Alcohol Spectrum Disorders: Feasibility Study.**
McCoy SW, Jirikowic T, Price R, Ciol MA, Hsu LY, Dellon B, Kartin D. (USA)
Publication - Phys Ther.
25th June 2015

162. **Effects of Developmental Alcohol Exposure on Potentiation and Depression of Visual Cortex Responses.**
Lantz CL, Sipe GO, Wong EL, Majewska AK, Medina AE. (USA)
24th June 2015

163. **Impairment of social behaviour persists two years after embryonic alcohol exposure in zebrafish: A model of fetal alcohol spectrum disorders.**
Fernandes Y, Rampersad M, Gerlai R. (Canada)
18th June 2015

Back to Table of Contents
164. Prenatal Alcohol Exposure is Associated with Regionally Thinner Cortex During the Preadolescent Period.
Robertson FC, Narr KL, Molteno CD, Jacobson JL, Jacobson SW, Meintjes EM. (USA, South Africa)
Publication - Cereb Cortex. pii: bhv131
17th June 2015

165. Choline Ameliorates Deficits in Balance Caused by Acute Neonatal Ethanol Exposure.
Bearer CF, Wellmann KA, Tang N, He M, Mooney SM. (USA)
Publication - Cerebellum.
18th June 2015

166. Embryonic alcohol exposure: Towards the development of a zebrafish model of fetal alcohol spectrum disorders.
Gerlai R. (Canada)
16th June 2015

167. Embryonic catalase protects against ethanol embryopathies in acatalasemic mice and transgenic human catalase-expressing mice in embryo culture.
Publication - Toxicol Appl Pharmacol.
11th June 2015

168. Antenatal alcohol exposure: An East Anglian study of midwives' knowledge and practice.
Anne Marie Winstone & Christopher Verity (UK)
Publication - British Journal of Midwifery
March 2015

Back to Table of Contents
1. **Fetal Alcohol Spectrum Disorders (FASD) and Confabulation.**  
   A REVIEW FOR CRIMINAL JUSTICE PROFESSIONALS  
   Jerrod Brown, MA, MS, MS, MS, Pamela Oberoi MA, Jeffrey Long-McGie, MA, MBA, Judge Anthony (Tony) Wartnik, BA, JD, Erv Winkauf, MA, Sarah Herrick, MA, LP, LPCC, CCFC

2. **Fathers drinking: Also responsible for fetal disorders?**  
   Source: Taylor and Francis  
   14th February 2015

3. **High Rates of Missed Diagnoses of Fetal Alcohol Syndrome.**  
   Health Day News  
   12th January, 2015

4. **Fetal Alcohol Syndrome Among Children Aged 7–9 Years — Arizona, Colorado, and New York, 2010.**  
   Deborah J. Fox, MPH, Sydney Pettygrove, PhD, Christopher Cunniff, MD, Leslie A. O'Leary, PhD, Suzanne M. Gilboa, PhD, Jacquelyn Bertrand, PhD, Charlotte M. Druschel, MD, April Breen, Luther Robinson, MD, Linnette Ortiz, Jaime L. Frias, MD, Margaret Ruttenber, MSPH, Donald Klumb, PhD, F. John Meaney, PhD  
   30th January 2015

5. **Study Identifies Impacts of Women's Socio-Economic Status on Infant Health.**  
   Brenda McNally, Press Officer for the Faculty of Arts, Humanities and Social Sciences  
   16th January 2015

   March 2015

[Back to Table of Contents]
A. Fetal alcohol test under development.
Article by Tracey Romero
Publication - The Philadelphia Inquirer
9th February, 2015

B. Fetal Alcohol Exposure Often Mistaken as Behavioral Issues.
Article by Neil Osterweil
Publication - Medscape Medical News
12th January, 2015

C. New warning over booze in pregnancy: Half a glass of wine ‘could stop some babies breathing’.
Article by Sophie Borland, Health Correspondent for the Daily Mail
24 February 2015

D. Das Fetale Alkoholsyndrom
Im Kindes- und Erwachsenenalter.
[Fetal Alcohol Syndrome: Alcohol, Pregnancy, and Risks for the Developing Child]
Spohr, Hans-Ludwig

E. Better-off women more likely to drink alcohol in pregnancy.
Article by Rachel Flaherty
Publication – the Irish Times
15th January 2015

F. Drinking in pregnancy 'significant' cause of childhood brain damage.
Article by Eleanor Bradford, BBC Scotland Health Correspondent
23rd June 2015

ITV Documentary
3rd March 2015

Back to Table of Contents
1. FASD in Denmark: What’s All the Fuss?

Janni Niclasen, PhD

Janni Niclasen, PhD, psychologist is an assistant professor at the Department of Psychology, University of Copenhagen, Denmark.

Her research focus is on prenatal exposure to low doses of alcohol on the one hand and neurodevelopmental outcomes on the other hand. She has a particular interest in research methodology and the strengths and limitations of different research methodologies.

Back in 2012 a series of studies conducted by a research group from Aarhus, Denmark, were published in the British Journal of Obstetrics and Gynaecology (BJOG), (Eriksen et al., 2012; Kesmodel et al., 2012b; Kesmodel et al., 2012a; Skogerbo et al., 2012; Underbjerg et al., 2012). The studies looked at the associations between prenatal exposure to low-moderate doses of alcohol and child neurodevelopment at age five. None of the studies reported negative associations between low-moderate doses of alcohol and child development. The results were not all that ground-breaking per se. Several previous studies had reported no such negative associations whereas other studies had reported negative associations indicating that exposure to low-moderate doses of alcohol indeed have negative consequences for the developing foetus.

The real reason that the studies received much attention was that a press release was sent out in relation to the publication of the studies with the headline “Danish studies suggest low and moderate drinking in early pregnancy has no adverse effects on children aged five” (British Journal of Obstetrics and Gynaecology, 2012). In the press release it was stated that up to eight drinks per week did not have any significant effect on the development of the children. In other words, the authors suggested that, drinking up to eight units of alcohol per week in early pregnancy had absolutely no consequences for the developing foetus. Below, I will first try to understand the results, that is, the lack of negative association between alcohol intake and child neurodevelopment. This will be done by looking at the socio-demographic and lifestyle factors of those who drink and those who do not drink alcohol in pregnancy. Secondly, I will look at the culture of Denmark in respect to alcohol and in relation to gender equality. With this as a starting point I will try to understand why Danes in general might be more reluctant to recommend abstinence compared to most other comparable countries.

To my knowledge all FASD studies conducted in Denmark in recent years show no negative associations between prenatal exposure to low doses of alcohol and child neurodevelopment (including studies conducted by myself and my co-authors). Many of the studies even report on a J-shaped association indicating that exposure to a little alcohol is actually beneficial to the developing foetus. Is this because a little alcohol is indeed beneficial to the exposed Danish children or do the results reflect other factors? In order to investigate this I decided to carry through a small descriptive study looking at a long list of lifestyle and sociodemographic factors of those women who drink and those who do not drink alcohol in pregnancy (Niclasen, 2014). The study was published earlier this year in the journal Alcohol and Alcoholism.

Data from the study derived from the Danish National Birth Cohort (DNBC) which is a large-scale cohort including information on more than 100,000 pregnancies. Out of these, data from 63,464 women who all had answered questions regarding their alcohol intake in pregnancy on three different occasions, were included in the study. The women were subdivided into exposure groups according to their self-reported alcohol intake measured on three occasions throughout pregnancy. The following categories were adapted: 0, >0-10,
>10-30, >30-90, >90 units of alcohol throughout pregnancy. The abstaining group reported drinking 0 units throughout pregnancy, the >0-10 group between >0 and 10 units and the high-intakers >90 units throughout pregnancy. The results revealed substantial differences between intake groups on virtually all parameters. The high intakers (N=5476) were older, more like to eat fish, have a pre-pregnancy Body Mass Index within the normal range, 6.5% had compulsory schooling only where as 21.2% of the women had a university degree. They were, on the other hand, less likely to watch television and drink cola. Conversely, the abstainers (N=7204) were younger, more likely to drink cola, watch television, smoke cigarettes, live alone, have psychiatric problems, 17.8% had compulsory education only, whereas 5.8% had a university degree. The abstainers were less likely to exercise and eat fish. To sum up, the group of high-intakers were much better educated and generally lived healthier lives compared to the abstainers and low intakers.

In order to understand the results of the Danish studies, I think we need to bear these descriptives in mind. Regardless of alcohol exposure in pregnancy I believe, as a child psychologist, that it is fair to say that children of mothers who live healthier lives and are better educated are more likely to have children who are neuropsychologically more well-functioning with more developed coping skills and with better emotional regulation. Such children, who are thriving psychologically are better able to handle stressful and challenging situations and this in turn lowers their risk for poorer mental health outcomes later in life. The opposite is true for the least educated with poorer lifestyles. Last year, in collaboration with my colleagues, I conducted a study looking at the association between prenatal exposure to alcohol and child development at age seven (Niclasen, Teasdale, Strandberg-Larsen, & Nybo Andersen, 2013). In the statistical analyses we controlled for what was considered to be the most important confounding factors, including maternal and paternal education, smoking and psychiatric disorders and maternal psychological well-being in pregnancy. The results revealed the most favourable outcomes for the high intakers (over 90 units of alcohol in pregnancy) and the least favourable outcomes for the children of the abstainers. Do these results imply that exposure to over 90 units of alcohol in pregnancy has a positive effect on a developing foetus? Or does it indicate a positive influence of other factors that are not controlled for in the statistical analyses? I think that the effect of upbringing is much greater compared to the potential effect of being exposed to a little alcohol. Because of the large differences on sociodemographic and lifestyle factors between the exposed groups it might be fair to say that potential (small) effects of being exposed to a little alcohol is masked by large differences on other factors that strongly influence child development.

Another important issue in relation to the findings is that the children in our study were assessed at age seven. It may be that age seven is too early for any potential effects to be present. Many of the potential deficits may not be evident until the teen years and adult life. For example, one study of 2,600 children with Foetal Alcohol Syndrome reported that about half had normal developmental scores at pre-school whereas all had severe brain dysfunction at age ten (Astley, 2010). In the same group of children 10 % were found to have attention problems at age five, whereas 60 % had attention problems at age ten. The lack of negative association in my study may thus be that the children were assessed at too early an age, because the behavioural effects may only manifest themselves later in childhood.

If this holds true we can ask whether similar conclusions can be drawn for the Aarhus studies? These studies actually also applied data from the DNBC. First, it seems plausible that large differences between exposure groups on sociodemographic factors are responsible for the results even though the Aarhus studies adapted different exposure categories (0, 1-4, 5-8, 9+ in early pregnancy). We might therefore ask whether it makes sense to send out a press release indicating that drinking up to eight units per week is not damaging for the developing foetus? Secondly, the children in the Aarhus studies were assessed at age five, i.e. even younger than was the case in my study (where they were assessed at age seven). It may therefore, very well be that the children were assessed at an inappropriate age span.

On this basis, I think that it is fair to conclude that the children of the large scale cohorts are followed into adolescence and adulthood in relation to prenatal exposure to low doses of alcohol.

The second question I recited above was why Danes are more reluctant to recommend abstinence compared to most other comparable countries and potentially why the press release was sent out stating that drinking up to eight units per week is all right. The official guidelines from the Danish health authorities is that they recommend abstinence. However, much scientific debate goes on in Denmark about the rationale for this considering we really have no empirical evidence to support abstinence (as opposed to for example, recommending up to two drinks per week). Denmark is a beer drinking nation, and the breweries of
Carlsberg and Tuborg are indeed both Danish. Around 5.5 million people live in Denmark out of which most drink alcohol on a regular basis. In fact only 7% of women and as little as 3% of men are all time abstainers. A standard drink in Denmark is defined as containing 12 gram of absolute alcohol, compared to 7.9 grams of absolute alcohol in a UK standard drink. Danish youth drink much more and have earlier debuts compared to youth from most other European and Scandinavian countries. 20% of the 13-year-olds have for example been drunk (defined as having had a minimum of five alcohol containing units on a single occasion), and they further drink much more per occasion compared to youth from neighbouring countries. More than six out of ten 15-year-old Danish girls have been drunk within the last month. And as was also the case for the pregnant women, people with tertiary education generally drink more than those less well educated.

In total, this adds up to an average yearly intake of 12 litres of pure alcohol per person per year (including all citizens aged 16 or above). It has been suggested that one of the reasons that Danes drink so much is that we make use of a combination of Nordic and Southern European drinking patterns. A Nordic drinking pattern is characterised by drinking alcohol on few occasions but with many drinks per occasion (getting drunk basically). This pattern can probably be traced back to the Vikings’ drinking bouts during which they drank large quantities of mead during the long and cold winters. On the other hand, we have adapted the Southern European drinking pattern characterised by drinking on many occasions but having few drinks per occasion. 

This pattern has been adapted since the 1950s when Danes started going on package tours to the Southern parts of Europe. This mix of drinking patterns thus means that Danes don’t just drink often, but also consume large quantities per occasion.

Apart from being a nation of alcohol, Denmark is also one of the most equalitarian countries in the world. Danes generally have a much higher focus on women’s rights. Denmark was one of the first countries to provide women with the right to vote (1915), and the first country to liberate pornography (1967). Denmark is also one of the countries in the world with the most favourable conditions regarding maternity leave. All parents receive a total of 52 weeks of maternity leave (12 weeks with full payment, and 40 weeks with reduced payment). There are free or low cost day-care for everyone allowing 79% of mothers to return to the work-force, most of whom return to their previous level of employment. Therefore, it is actually possible for women, in most respects, to continue with their old life even after having had children – something which even holds true for single mothers.

On top of this, Denmark is rated the happiest nation in the world according to the World Happiness Report (Helliwell, Layard, & Sachs, 2013). This report is summed up by different scales including healthy life expectancy, social support and freedom to make life choices. Equalitarianism and gender equality is beyond doubt part of the reason for the top ranking on the World Happiness Report. But what about alcohol? Could it be that the liberal attitudes towards alcohol is also an important reason for the top ranking? I actually think it might be. But I also speculate that this mixture between liberal attitudes toward alcohol, gender equality and happiness cause Danes to be more reluctant to give up their old lifestyle in relation to being pregnant. Telling women that they are not allowed to drink (while the fathers-to-be still can) is like touching upon something sacred, namely gender equality. Is this why there is much resistance when the health authorities recommend pregnant women to change their lifestyle (including alcohol intake)? I think that the issue of gender equality is indeed very important. However, as a child psychologist I also believe that in this context we need to focus less on the individual rights of the women and on equalitarianism and more on the rights of the unborn children. Truly, we do not have the empirical evidence that having a glass of wine on a Saturday night during your pregnancy is actually harmful to the developing foetus – but on the other hand we don’t either have empirical evidence that it is beneficial for the developing foetus.

Reference List
British Journal of Obstetrics and Gynaecology. (2012). Danish studies suggest low and moderate drinking in early pregnancy has no adverse effects on children aged five.
Ref Type: Online Source
Ref Type: Online Source
2. Assessing Children with FASD

Judith K. Eckerle Kang, MD

Judith K. Eckerle is an Assistant Professor of Pediatrics and the Director of the Adoption Medicine Program at the University of Minnesota. Dr. Eckerle sees children from foster care, domestic and internationally adopted children in the Adoption Clinic as well as in the Fetal Substances Exposures Clinic.

I was adopted from Seoul, South Korea as a baby and grew up with my family in the USA as the only adopted child in a family of 6. My mother went back to college when I was school-age and I accompanied her to the chemistry and science classes during my school breaks. I knew that someday I would be a doctor. I shadowed a prominent physician, Dr. Dana Johnson, in the neonatal intensive care unit (NICU) during my senior year of high school.

Years later, while in medical school, a relative adopted a child from Korea and told me that there was an adoption clinic that I should look into. I contacted the physician, and it was Dr. Johnson who had done both adoption medicine and NICU for years. I came to do an adoption rotation with him and after 3 days, I knew I would do adoption medicine for my career. The thought of working with adoptive families and their children, resonated with my own background and history. After my pediatrics residency in NYC at Cornell Medical Centre, with the help of Dr. Johnson, Dr. Michael Georgieff and Dr. Maria Kroupina, I did a 1 year post-doctoral adoption research fellowship in the Center for Neurobehavioral Development (CNBD) at the University of Minnesota prior to starting my career.

Once I started my job, in reviewing pre-adoption records, speaking with adopting families and assessing the children in clinic, I realized that many children in the adoption system are also exposed to prenatal substances. Because of this, I started to learn more and train in Fetal Alcohol Spectrum Disorder (FASD) and I began to collaborate with the regional organization, Minnesota Organization on Fetal Alcohol Syndrome (MOFAS). I discovered that there was an enormous gap in the number of knowledgeable medical practitioners for children who were exposed to prenatal substances.

Some of these children have FASD or other prenatal exposures but the basic FASD assessment of face, growth and exposures may miss many other contributing medical problems that may be exacerbating their learning or behavior issues.

Back to Table of Contents
We also look for the following:

1) Infectious disease testing: many children have backgrounds that require testing for sexually transmitted illness, tuberculosis risk factors.

2) Vitamin deficiencies: there is a high percentage of children that we have assessed in our clinic with vitamin D, iron or micronutrient deficiencies.1-3

3) Patients with learning problems, internalizing or externalizing behaviors can have hypo or hyperactive thyroids.

4) Other genetics or syndromes: We screen for fragile X, chromosomes or microarray as other syndromes that can mimic the problems seen in FASD.

5) Developmental delays including sensory processing disorder: Children with problems with handwriting or with their sensory development can appear hyperactive or out of control but can be addressed with home, school or medically based therapies.

Our assessments of these children include developmental screening with a pediatric occupational or physical therapist, the medical visit for a full clinical assessment, neuropsychology testing to identify their academic and functional strengths and weaknesses, and psychology counselling to help the families and children understand one another and work together. Whether domestically or internationally adopted, most of these children come from backgrounds of high stress, early adversity, exposures or other traumas. All of this should also be addressed when assessing the child with prenatal exposures.

My interest in FASD has led to collaborations with the psychology and psychiatry departments at my University. We have completed the first stage of a randomized, double blind, placebo controlled trial of choline supplementation in children with prenatal alcohol exposure, based on prior animal studies that showed cognitive improvement after supplementation with this vitamin. Our initial results have shown some promise for children with prenatal alcohol exposure.

While in the past, FASD has been felt to be a static disorder. There are a number of medical, nutritional, psychological and developmental interventions that can potentially improve their overall health status and self-esteem. I’ve been truly moved at how a comprehensive approach to these children, can help schools and families to get on a much brighter path to help these children reach their full potential. This is why I have chosen to focus my career on helping adopted children and children with prenatal exposures.

**Reference List**


[Back to Table of Contents]
3. Facing Fetal Alcohol Spectrum Disorder in Italy

Mauro Ceccanti, Daniela Fiorentino and Mario Vitalli

Mauro Ceccanti, Associate Professor, Clinical Methodology, University La Sapienza, School of Medicine, Rome. Director of Alcohol Referral Centre, Lazio Region

Scientific Activity
353 scientific papers, 115 congress talks, and edited about 30 books.

Main Research Lines
Alcohol Use Disorder: Neurobiology, Clinical features, Treatment, Fetal Alcohol Syndrome (FAS)

Scientific Societies:
President of Italian Society for Fetal Alcohol Spectrum Disorder and the Treatment of Alcoholism and its Complications.

Daniela Fiorentino, psychologist, Lazio Regional Center for Alcohol, coordinated the Italian study of prevalence and participated in several FASD clinic around the world (South Africa and US). She studies psychosocial factors involved in health promotion and alcohol related problems prevention.

Mario Vitali, MD
Psychiatrist, Consultant of Psychiatry at Alcohol Addiction Program, Policlinico Umberto I, Sapienza University of Rome directed by Prof. M. Ceccanti

Introduction
In 2010, about 60% of the childbearing-aged female population in Italy declared that they consume alcoholic beverages at least once a year (ISTAT, 2011). Italian National guidelines for healthy nutrition recommend women to avoid drinking any amount of alcohol during pregnancy (INRAN, 2003). Anyway despite this official recommendation, risks related to alcohol consumption in pregnancy are still undervalued in Italy, including also the professionals devoted to woman and child’s care. Drinking one glass of wine or beer occasionally during pregnancy is considered safe by 50% of Italian neonatologists interviewed in a national survey (Vagnarelli et al., 2011). And while in other European countries warning labels on alcoholic beverages are now mandatory, Italy has not enacted such a law yet.

Alcohol and pregnancy in Italy

Efforts to evaluate the effects of alcohol consumption during pregnancy in Italian samples have given mixed results. Part of the Italian studies did not find any associations between drinking and low birth weight at birth (De Nigris et al., 1981; Primasteta et al. 1993; Parazzini et al., 1994; Parazzini et al., 1996). Links between smoking and drinking and low birth weight were found by others (Lazzaroni et al. 1993a; Lazzaroni et al., 1993b). Among a population of 4,966 women, Bonati and Fellin (1991) found that low birth weight was not related to moderate maternal drinking, but the association occurred for heavy, out of meal, drinking. Chiaffarino (2006) showed a significant association between the consumption of 3 or more drinks per day and children small for gestational age, but no associations were found for lower quantities. Recently, in a case control study, De Marco et al (2011) suggests alcohol as a leading risk factor for bifid cord.

Data from a survey performed in an antenatal clinic in a major hospital in Rome, showed that more than 35% of the women interviewed (N=991) drank during pregnancy, mostly wine and beer. Frequency of consumption decreased by trimester: from 13,5% drinking at least 4 times a week in the first trimester to 6,4% in the second and 3,6% in the third one. 7,2% of the total sample drank both out and in meals. Among
those drinking during pregnancy, 7.4% had at risk consumption (7 or more drinks per week) and 3.7% drank 3 or more drinks in a single occasion, at least once during pregnancy. Women were also asked to answer to the question “How many drinks does it take to make you feel high?”, as stated in the T-ACE questionnaire: 44.9 scored positive (more than 2 drinks) (Fiorentino et al., 2012)

Italian papers describes a total of 25 children in 7 different studies: description of these cases corresponds to those described in international literature (Calvani et al., 1985a; Calvani et al., 1985b; Moretti & Montali, 1982; Pensiero et al., 2007; Roccella & Testa, 2003; Scianaro et al., 1978; Scotto Di Tella et al., 1993).

**Fasd prevalence and features in Italy**

Among prevalence studies, those based on an active case ascertainment methodology, give more accurate results and the highest prevalence rates: in these studies researchers actively evaluate a population on the field to individuate cases (May, 2009).

A particular kind of active strategy is represented by the in-school active case ascertainment studies where all the children attending a number of randomly selected school are evaluated, usually those attending the first grade (6-7 years old) in a context of general population (May, 2010).

Among such a kind of studies those performed in South Africa (May et al., 2000, 2007, 2013; Viljoen et al., 2005) gave rise to the highest prevalence, for the extremely poor condition of life in the areas chosen for the studies. But also studies performed in western middle socio-economic status countries got to unexpectedly high percentages of prevalence for the western world.

Excluding those performed in South Africa, a recent meta-analysis resumes FAS, PFAS and ARND prevalence rates found in in-school studies, as follows (pooled estimate): FAS = 3.6 per 1000; PFAS 29 per 1000; ARND=2.3 per 1000 [Ospina, 2013].

Between 2003 and 2006 Italy performed the first in-school active case ascertainment study in general population performed in Europe (Aragon et al., 2008; Ceccanti et al., 2007; Fiorentino et al., 2007; Kodituwakku et al., 2006: May et al., 2006; May et al., 2011; Ceccanti et al., 2014)

A total of 976 first grade children were screened (parents’ consent rate 50%). The evaluation went through three different steps (May et al. 2000; Fiorentino et al. 2006): 1) height, weight and head circumference were screened. And behaviour and pre-learning skills were evaluated. Children found below the tenth percentile for growing measures or showing behavioural or learning problems entered the second step. Mothers were interviewed on lifelong health, alcohol use at present, during the three trimesters of the indexed pregnancy and before it. 2) Selected children were given the dysmorphic exam and neuropsychological testing. 3) During the third step all data were merged to get to a final diagnosis. After having merged all the available data, 46 children (4.7%) were identified as falling into the FASD spectrum: 8 FAS (0.8%);36 Partial FAS (3.7%); 2 ARBD and ARND (0.2%).

As expected, FASD children, compared to 116 randomly selected controls, were smaller for height, weight and head circumference and showed a higher score on dysmorphism index (a weighted measure of the presence of dysmorphic features).

Neuropsychological profile revealed that FASD children scored lower in verbal performance and total IQ, compared to controls. Their performances were poorer in non-verbal reasoning (Raven), language comprehension (Rustioni) and pre-learning skills (IPDA) as well. FAS children showed more attention issues than controls, as resulting from SCOD score.

Focusing on maternal alcohol consumption, 25% drank during pregnancy at least 5 days per week and 15% drank at least 7 drinks per week. A comparison of current drinking (at the time of the interview) between FASD mothers and controls showed a significant difference (p<0.001) in the mean number of drinks consumed per week (FASD Mean=10.37 SD 18.92; Controls Mean=1.52; SD=2.80). Current drinking could be a more reliable measure of drinking because less influenced by social stigma.

**Risk factors**
The most important risk factor for FASD is the quantities of alcohol consumed and while a safe threshold of consumption has not been established yet, literature indicates a mean consumption of more than one drink per day (14 g of alcohol nearly) as at risk (Hankin & Sokol, 1995). Binge drinking is considered the most risky condition, as the highest the BAC the highest the damage (May, et al., 2007). During pregnancy the consumption of three or more drinks in a single occasion is highly related to morphological and behavioral evidences of damage in children (May, et al., 2007).

The typical Italian style of consumption, mainly wine at meals, led to study whether a difference occurs in the damage caused by alcohol, depending on the kind of alcoholic beverage ingested, in an animal’s model (Ceccanti et al., 2010). This hypothesis was tested comparing mice exposed perinatally to ethanol at 11% vol or to red wine at the same ethanol concentration. Prenatal ethanol exposure produces severe changes in brain, liver, and kidney through mechanisms involving growth factors. These molecules regulate survival, differentiation, maintenance, and connectivity of brain, liver, and kidney cells. Despite the abundant available data on the short and mid-lasting effects of ethanol intoxication, only few data show the long-lasting damage induced by early ethanol administration. This study shows that, in aged mice, early administration of ethanol solution induced long-lasting damage at growth factor levels in frontal cortex, hippocampus, and liver but not in kidney. Otherwise, in mice exposed to red wine, significant changes were observed in the liver and kidney but not in the hippocampus and frontal cortex. The brain differences in ethanol-induced toxicity when ethanol is administered alone or in red wine may be related to compounds with antioxidant properties present in the red wine.

Many other factors contribute to produce a damage: mother’s age, gravidity, parity, body size, nutritional status, socioeconomic status and other drugs use, as well as genetic and epigenetic factors (Abel et al., 1995; Roberts & Nanson, 2000; Ebrahim et al., 1999; Jacobson et al., 1993).

Data from the antenatal screening for drinking behaviour of pregnant women attending a major hospital in Rome showed that the most recurrent risk factors, significantly correlated with a number of variables measuring drinking behaviour (i.e. drinking more than one drink per occasion, positive score to the tolerance question, number of alcoholic beverages consumed) were: being younger (under 30), having an unplanned pregnancy, being unemployed, having a lower educational qualification and being single (Fiorentino et al., 2012).

The role of paternal alcohol exposure (PAE) on offspring EtOH sensitivity and neurotrophins has not received much attention. In a recent Italian study (Ceccanti et al., 2015) the authors examined whether PAE may disrupt nerve growth factor (NGF) and/or brain-derived neurotrophic factor (BDNF) and affect EtOH preference/rewarding properties in the male offspring. CD1 sire mice were chronically addicted for EtOH or administered with sucrose. Their male offsprings were assessed when adult for EtOH preference by a conditioned place preference paradigm. PAE affected NGF levels in frontal cortex, striatum, olfactory lobes, hippocampus and hypothalamus. BDNF alterations in frontal cortex, striatum and olfactory lobes were found. PAE induced a higher susceptibility to the EtOH rewarding effects mostly evident at the lower concentration (0.5 g/kg) that was ineffective in non-PAE offsprings. Moreover, higher ethanol concentrations (1.5 g/kg) produced an aversive response in PAE animals and a significant preference in non-PAE offspring. PAE affects NGF and BDNF expression in the mouse brain; PAE may induce ethanol intake preference in the male offspring.

Preventive efforts

Data from the cited Italian study of prevalence revealed that among all the mothers of children enrolled in the screening, 65% did not receive any suggestions from professionals about drinking during pregnancy. Hence, preventive efforts should be targeted at disseminating correct information about risks related to alcohol consumption in pregnancy both among professionals and general population.

A universal preventive intervention aimed at enhancing risk awareness related to alcohol consumption in pregnancy in health professionals and pregnant women, was performed in two health districts in Rome in 2013 (Fiorentino et al., 2014). Five different actions were undertaken: 1) Creation of a 20 minute educative documentary including information and showing counselling sessions with a pregnant currently drinking woman and the dysmorphology exam; 2) delivery of two Continuing Medical Education courses addressed to gynaecologists, obstetricians, nurses, pediatricians, psychologists and social workers; 3) questionnaire’s administration to pregnant women attending obstetric facilities, to investigate alcohol consumption and information on FASD; 4) pamphlets and posters dissemination in obstetric facilities; 5) final questionnaire’s
administration to control campaign’s penetration. During the intervention, 87 health professionals were trained, 1700 pamphlets and 50 posters were disseminated in health facilities. DVDs containing the documentary were delivered to all courses’ attendees. Results from the questionnaire delivered to pregnant women attending health facilities (N = 340) showed that professional’s suggestion can prevent alcohol consumption during pregnancy: women told not to drink, did not drink compared to those suggested only to reduce drinking (p<.001). Moreover, knowing about FASD could be a protective factor. In fact, women who could correctly identify it, did not drink, compared to those that did not know what it is (p<.005). And women who had seen some preventive materials drank less compared to those who had never seen leaflets or other preventive messages (p<.005)

After the dissemination of leaflets and pamphlets, exposition to the preventive message enhanced from 39% to 58% and 74% could correctly remembered it. After having read leaflets and posters, 86% of drinking pregnant women gave up and 14% cut on quantities. None of them kept on drinking.

An International campaign to raise awareness of drinking during pregnancy is being now underway in Italy and other countries in Europe in collaboration with EUFASD Alliance (Bazzo, 2014). To reinforce the capacity of individuals and community in making health choice is a key goal. Its effectiveness will be evaluated in several countries around the world.

Conclusions

Data from the in school screening for FASD in Italy revealed an unexpectedly high prevalence. Awareness of the risks related to alcohol consumption in pregnancy is not widespread yet and also most of professionals still believe that risks exist only in case of heavy drinking. Universal preventive initiatives, such as information dissemination and health advises, represent cost-effective interventions, among not-clinical population. Pregnancy represents a fertile moment for disseminating health preventive messages as women are highly motivated to protect their babies’ health and take into great account professionals’ advises.

In last years in Italy, thanks to the spreading of the results of the in school screening for prevalence, initiatives to prevent alcohol exposed pregnancies are growing. Lazio Local Government, after having funded the prevalence study, funded the FASD Observatory established in a major hospital in Rome. Main objectives are: improvements of diagnostic ability in identifying FASD cases; monitoring cases in the long term; to establish FASD incidence and prevalence; epidemiology of consumption during pregnancy. Hopefully this work will lead to an improvement of selective and indicated interventions for FASD prevention and treatment.

Bibliografia


INRAN (Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione), *Linee guida per una sana alimentazione italiana*, Revisione, 2003


www.nofas-uk.org

41


Ospina M, Dennett L. *Systematic Review on the prevalence of Fetal Alcohol Spectrum Disorders*. IHE Institute of Health Economics, Alberta, Canada. April 2013


Back to Table of Contents
4. Rehabilitation for Children with Fetal Alcohol Spectrum Disorders (FASD) - A Unique Opportunity to Create a Holistic Forecast

Dr. Heike Hoff-Emden
Pediatric, Psychotherapist and qualification in EMDR
Member in expert commission „FAS-Guidelines in Germany”
Head doctor in social pediatric centre in Leipzig

Having worked with people (predominantly children) affected by FASD for more than 20 years, I have become increasingly aware of the need for specialist interventions to improve the quality of life for children with FASD and their families. As recent as 2012 caregivers and parents raising children diagnosed with FASD felt very much "left alone" with their problems. No specific FASD educational programmes or concepts for therapy were available in Germany and so the necessity of a specialist neurological rehab centre for FASD became apparent. Caregivers and parents needed and indeed longed for this kind of facility - a centre where the staff have a great knowledge about FASD and where the types of therapy available are tailor-made for those undergoing rehabilitation.

In the light of these circumstances approximately 300 children, adolescents and young adults diagnosed with FASD were admitted to the neurological rehabilitation centre between July 2012 and April 2015.

Before discussing further details of the programme, I would like to explain a little more about the term "paediatric rehabilitation" as defined in the context of the German healthcare system.

Who is eligible for paediatric rehabilitation? What is its purpose? And when is paediatric rehabilitation considered necessary? Paediatric rehabilitation is available to children, adolescents and young adults from birth to the age of 27. Its aim is to eliminate serious threats to health or to considerably improve impaired health (physical or mental). This type of rehab is considered necessary when a disease has side effects that could have a negative impact on future employment or when assistance is needed to strengthen the individual's ability to participate in social activities.

The multidisciplinary, personalised rehab programme takes a holistic approach as illustrated in the following table (Fig. 1).

Fig. 1 - Multidisciplinary, Personalised Rehab Programme
<table>
<thead>
<tr>
<th>Therapy or educational component</th>
<th>Target or content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiotherapy</td>
<td>Body perception</td>
</tr>
<tr>
<td>Music therapy</td>
<td>Non-verbal communication</td>
</tr>
<tr>
<td>Neuropsychology</td>
<td>Testing and training</td>
</tr>
<tr>
<td>Occupational therapy</td>
<td>Formulating a plan of action</td>
</tr>
<tr>
<td>Neuropedagogy (Educational Neuroscience)</td>
<td>Improve perseverance and concentration</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>Trauma therapy</td>
</tr>
<tr>
<td>School</td>
<td>&quot;Finding the right educational path&quot;</td>
</tr>
<tr>
<td>Career counselling</td>
<td>Trial work opportunities; job preferences and skills</td>
</tr>
<tr>
<td>FASD Seminars for parents / for children</td>
<td>Information about FASD</td>
</tr>
<tr>
<td>Acceptance and &quot;coping&quot;</td>
<td>Discussion with and for caregivers and those affected by FASD</td>
</tr>
<tr>
<td>FASD-Diagnostics/One-to-one conversations</td>
<td>The issue of a socio-medical assessment; identification of capabilities and resources</td>
</tr>
</tbody>
</table>

Quality and standards play an important role and as part of her bachelor's dissertation "An Analysis of the Sustainability of the Rehabilitation Concept and FASD Seminars as Practiced in the Rehabilitation Facility KMG Sülthayn" Nina Reichenbach evaluated the rehabilitation process. Here is a brief summary:

**Method:**
A survey was carried out involving 49 rehabilitants, foster and adoptive parents based on a modified KINDL questionnaire to assess the health-related quality of life.

**Hypotheses:**
1. The overall concept implemented at the rehab facility considerably improves the outlook for patients with this condition.
2. Parents and rehabilitants alike (self-assessment) establish a reduction in challenging behaviour after rehab.
3. Discussion and exchange were helpful when coming to terms with the diagnosis and led to a better understanding thereof.

**Results:**
Fig. 2 - Mean Values Obtained from the Assessment of Named FASD Specific Interventions
Fig. 3 - Mean Values Showing Improvement in the Categories Emotions, School, Family and Friends

Fig. 4 - Relative Frequencies According to the Children's Assessment
Summary of the Results:
FASD specific interventions proved helpful. Negative behaviour was observed less frequently after rehab. Both the quality of life in general and the quality of family life improved.
The children themselves noticed improvements: they experienced positive emotions, felt the quality of life was better; they had more fun, experienced less anger, had less arguments and fewer problems at school.

The talks and conversations about FASD (accepting and coping) and the socio-medical assessment were deemed the most important interventions.

One point of criticism was the limited time available for schooling.

**Conclusions:**

Inpatient rehabilitation is a unique opportunity and must be recognized as such. In addition to the advantages of a multi-professional context for observation, this type of rehabilitation provides customised treatment and enables rehabilitants and their families to discover their own resources. The concluding socio-medical assessment and neuropsychological testing are two key elements of the rehabilitation programme and contribute enormously to its success. Time spent together with physically disabled children is a valuable and important experience for those affected by FASD as it helps to develop social skills.

Another extremely important aspect of inpatient rehabilitation is being able to experience fellowship in a sheltered environment i.e. getting to know other people affected by FASD, making friends and feeling accepted.

The clinical setting is ideal to optimise medication or to begin treatment of other co-morbid conditions such as sleep problems, PTSD or behaviour disorders. This practice frequently leads to significant stress reduction not only for individuals undergoing rehabilitation but also for their caregivers.

In addition the clinic provides coordinated aftercare services including for example, the evaluation of results, FASD specific training programmes and cooperation with the judiciary.

There is no cure for FASD and problems do not disappear during the transition from childhood to adulthood. Adults affected by FASD need assistance even with basic living skills. It is imperative to identify and coordinate appropriate services and resources.
Individuals affected by FASD and their caregivers can only "survive" by connecting with others - networking is the key.

Children diagnosed with FASD often have a creative vein and during the **FASD Seminars for Kids** they are encouraged to express their feelings through art. The following drawings are a representative sample of the children's work.

The first picture is entitled "Hopes for the Future" and is self-explanatory.

All children dream about what they would like to do or be when they grow up - in this respect children with FASD are no different. But there is a grave difference and that is **living** with FASD. It is of utmost importance to do a "reality check" at an early stage - establish what kind of professional qualification can be achieved i.e. capabilities, ascertain where interests lie and think about what type of accommodation will be needed in the future.
Dealing with anger is one of the most difficult problems facing those affected by FASD. These explosive outbursts of rage are caused by overload and trauma-related dissociative disorders. There is no "one" solution to this problem. With the help of a therapist each individual affected by FASD must develop his/her own strategy for dealing with anger.

One of the main aims of the FASD Seminars for Kids is to facilitate disability acceptance and awareness. The child who drew this picture obviously felt the need to explain a little more and wrote:
"Build bridges - Chaos in your head - Helpers - We're wired differently"

During their stay at the rehab facility children gradually start to understand what it means to have FASD. This is the first step in a long process towards awareness and acceptance. Often they make friends for the first time ever - these friends have a lot in common!

When it comes to prevention campaigns the best ambassadors are those who are affected by FASD. Art is a good way of coming to terms with personal difficulties and often youngsters diagnosed with FASD want their pictures to be shown in public i.e. during lectures etc. in order to raise awareness about FASD.

The text reads:
"I ask you please to not drink alcohol!!!!!!!!!!

It's me
It's dangerous (spelling error) for the baby"

Message from the mother:
"Please don't drink alcohol during
The German word for pregnancy is actually "Schwangerschaft"; ironically "schwanken" means to stagger!

The rehabilitation clinic belongs to a business group currently in a phase of re-structuring and the Group Executive Committee chose to discontinue this well-established rehabilitation programme as of May 2015.

I shall continue to use my professional experience with FASD and with the help of my team will be setting up an FASD Centre for Excellence at the Social Paediatric Centre in Leipzig. This centre will be open to individuals affected by FASD; the FASD seminars for parents and children will resume.

Correspondence Address:
Dr. med. Heike Hoff-Emden

Sozialpädiatrisches Zentrum Leipzig
Delitzscher Strasse 141
Haus 51
D-04129 Leipzig

Telephone: +49 341 984690
Fax: +49 341 9800645
Email: spz@fhle.de

References:
Reichenbacher, N. Untersuchung zur Nachhaltigkeit des Reha-Konzeptes und der FASD Seminare in der KMG Klinik Sülzhayn, Entwicklung und Auswertung eines Evaluationsfragebogens, Bachelorarbeit SRH Gera(8/2014)
5. What can we learn from cross-cultural research on alcohol use in pregnancy?

Lisa Schölin BSc, MSc, AFHEA

Lisa Schölin is currently writing up her PhD a cross-cultural comparison of alcohol use in pregnancy in England and Sweden, at Liverpool John Moores University. She completed an undergraduate degree in Public Health Science and a master’s degree in Public Health Research Methods in her home country Sweden before moving to England in 2011 to complete a master’s degree in Public Health Science. She moved to England to gain a wider perspective on public health and subsequently she became interested in the way that policy influences people’s lifestyles and behaviours. Her main research interest is women’s alcohol consumption, specifically what changes pregnancy brings in alcohol habits and the rationale for drinking or abstaining during pregnancy.

Whenever I meet someone who asks what I do, and I tell them that I research alcohol and pregnancy, they tend to respond “well you shouldn’t drink when you are pregnant, doesn’t everyone know that?”. In my research I have explored practices and views on drinking during pregnancy in England and Sweden, with focus on the differences in policy in the two countries. Sweden endorses complete abstinence while the NICE guidelines in England states that women should avoid alcohol, however limit their intake to one to two units once or twice per week after the first trimester if they choose to drink. Interviewing both women and their partners in the two countries highlighted that the abstinence message appears engrained in the Swedish society, which forms strong social norms against pregnant women drinking alcohol. On the other hand, parents in England expressed views about abstinence being the safest option but some also discussed drinking small amounts and lack of evidence that small amounts would put the baby at risk.

My background in Public Health Science encouraged me to design my research project in accordance with a theoretical model which views alcohol and pregnancy not only as an outcome of psychological processes and individual behaviour, but more so as a result of interaction between the individual, friends, family, health professionals, society and norms, and public health policy. The Socio-Ecological Model of Health builds on the notion that the interaction between levels of factors (originally defined as micro, meso, and macro level by Bronfenbrenner in the 1970s) and provide some explanation why some women may choose to drink while they are pregnant.

My research adopts a mixed methods design; interviews with parents and midwives were used in conjunction with a survey to determine prevalence of alcohol use during pregnancy. The results from the survey show difference in reported alcohol use in pregnancy; in the third trimester 98.4% of Swedish women reported “never” drinking compared to 74.3% of English women. In addition, the results from the qualitative phase suggests that the attitudes among Swedish parents focus on the rights of the foetus to not get exposed to alcohol, which was contrasted to the woman’s right to decide over her own body among several English parents. These results are interesting in relation to the perception of advice received in maternity services, where English parents had different experience on what the official guidance is. Some had been told to abstain completely, some were given recommendations about limiting intake, and a few even described conflicting advice from different health professionals. Swedish parents on the other hand were unified in the experience that midwives promoted complete abstinence.
I find these results interesting; yet again relating to my underpinning philosophy of public health I also believed that the picture would be incomplete without exploring the views of midwives. I interviewed midwives working in Merseyside in England and Örebro County in Sweden, and again found disparities in the attitudes towards this topic. Swedish midwives were convinced that abstinence is the best way to avoid risks for the baby. Several mentioned research suggesting even small amounts could harm the baby. All English midwives were firm on the point that complete abstinence was the advice they give, yet some referred to the lack of evidence for drinking small amounts and their personal opinion that perhaps one drink would not harm the baby. Regardless of their opinion, they would still recommend abstinence.

While the results show that midwives promote the abstinence advice, interviews with parents also showed that there may be inconsistencies in what advice is given. As an example, I interviewed one woman who had researched the recommendations and drank within the weekly limit as advised by NICE. However, when meeting her midwife for her booking in appointment she was told she should not drink at all. Later in pregnancy, she was told by another midwife that having a glass of wine was fine. Whilst all English midwives interviewed said they recommend abstinence, they also highlighted that there may be variations in what advice other midwives give due to what the NICE guidance states. One midwife specifically called for abstinence advice at the policy level to be consistently communicated:

“I think the government should be saying “don’t drink”, no alcohol is safe during pregnancy it’s not safe to drink because we don’t know actually what the risks are. Well we know what the risks are but we don’t know what level would be at risk, so I would give the information, I think that we should all be singing from the same hymn sheet”

The cross-cultural approach of my research has allowed me to see how policy seems to influence women's decision to change their alcohol habits. The important point is that alcohol can be harmful to the developing baby and midwives acknowledge this. In my study it became clear that midwives put great emphasis on public health aspects of maternity care and that they felt that it is part of their role to discuss alcohol, along with other lifestyle behaviours. Furthermore, most women I interviewed who continued to drink were informed about the guidelines and would be very careful to ensure the amount they had did not exceed the recommended limit. I think that we need to recognise that women want the best for their baby and will make informed decisions based on the information they are given. More research is needed to further explore the discrepancy I found in my research, where midwives consistently give the abstinence advice and emphasise that no alcohol is the safest option but some women describe inconsistent advice.

So to the question on whether abstinence is a given among pregnant women my research indicates that the perception varies between countries that have endorsed a complete abstinence policy and a countries which in addition recommends a limit of consumption. It seems that the policy level impacts women’s decision on alcohol, yet it is only part of the equation. Following on from this research, future studies need to look further into women’s rationale for drinking where social norms need to be taken into account, other information sources they use to make these decisions, and how maternity services can best give information to expectant parents.

Contact details:

Lisa Schölin BSc, MSc, AFHEA
PhD Student
Liverpool John Moores University
Henry Cotton Building 15-21 Webster Street, Liverpool, L3 2ET
e: L.A.Scholin@2012.ljmu.ac.uk t: 0151 231 4441
6. **MicroRNA Biomarkers for the effects of fetal alcohol exposure.**

Rajesh C. Miranda, PhD.

**Rajesh C. Miranda** is a Professor of Neuroscience and Experimental Therapeutics at Texas A&M Health Science Center, College of Medicine. He completed his PhD in Neurobiology and Biopsychology at the University of Rochester, Rochester, New York and his post-doctoral training in Neuroendocrinology at Columbia University, College of Physicians and Surgeons, New York, NY. He joined the Faculty of the Texas A&M Health Science Center, College of Medicine in 1995.

Dr. Miranda directs a research laboratory in developmental neurobiology and epigenetics. His research focuses on the role of the maternal-fetal environment and drugs of abuse like ethanol in shaping fetal brain development. His research has been supported by the National Institutes of Alcohol Abuse and Alcoholism (NIAAA), Mental Health (NIMH), and Neurological Disorders and Stroke (NINDS).

Dr. Miranda has served as both a full and ad-hoc member for several National Institutes of Health, Scientific review panels, including Neurotoxicology and Alcoholism (NAL), and as a member and chairperson of the AA-4 study section. He served as the 2011-2012 president of the Fetal Alcohol Spectrum Disorders (FASD) Study Group, an affiliate of the Research Society on Alcoholism. Since 2012, Dr. Miranda has served on the Steering Committee for FASD prevention at the Texas Office for the Prevention of Developmental Disabilities.

The Fetal Alcohol Syndrome (FAS), which includes a range of craniofacial defects, as well as neurobehavioral and growth deficits, was first defined more than forty years ago (Jones et al., 1973; Lemoine et al., 1968). Since then, we have made significant progress towards understanding the consequences of heavy maternal alcohol consumption during pregnancy on fetal development and on the consequences of neurodevelopmental disability on child health and welfare. We also now understand that alcohol exposure during pregnancy can result in deficits that range in severity, and that FAS represents the severe end of a spectrum of deficits that are collectively termed the Fetal Alcohol Spectrum Disorders (FASD, (Riley et al., 2011)). However, we have made little to no progress towards preventing FAS.

In this article we will discuss data showing that fetal alcohol exposure continues to be a significant problem worldwide, because socio-cultural factors diminish the impact of standard prevention strategies. We argue for the adoption of a medical model for preventing FASD, with increased focus on early diagnosis. However, FASD is difficult to diagnose. Not only is it often difficult to document a history of prenatal exposure (May et al., 2013), but classical diagnostic signs including low birth weight, decreased cranial size and defects associated with the mid-face, are present in only some FASD infants and children. Even heavily exposed children with neurodevelopmental impairment do not exhibit readily identifiable craniofacial features that are consistent with diagnostic categories within the FASD continuum (Diwadkar et al., 2013; Jacobson et al., 2008). There is a clear need for better diagnosis.

A class of small non-protein-coding RNAs called microRNAs (miRNAs) that are secreted by cells and tissues
into a variety of body fluids including plasma offers a promising new approach to early diagnosis. Our data from a sheep model for three trimester-equivalent binge alcohol exposure show that plasma miRNAs in both the pregnant mother and neonatal lamb are sensitive to maternal alcohol exposure. Some of these sensitive plasma miRNAs are highly enriched in the developing and adult brain while the placenta is a likely source of other sensitive plasma miRNAs in both mother and neonate. We find that early developmental alcohol exposure also alters the expression of these brain-enriched miRNA in fetal neural stem cells. Moreover, manipulating specific brain-enriched miRNAs results in anatomical deficits like microcephaly, which mimic effects of fetal alcohol exposure. We argue that plasma miRNA profiles will have predictive value as biomarkers for effects of fetal alcohol exposure.

1. **Fetal alcohol exposure continues to remain a significant and world-wide public health problem:** The prevalence of fetal alcohol syndrome (FAS), the extreme end of the FASD continuum, varies from 0.05-0.2% in the US (May and Gossage, 2001), to 6-9% in South Africa (May et al., 2013). A diagnosis of FAS captures only a fraction of the estimated population of fetal alcohol-affected children. Prevalence estimates for the full spectrum, i.e., FASD range from 2-5% of the school-age population in the US and Western Europe (May et al., 2009) to ~14-21% in South Africa (May et al., 2013). FASD prevalence estimates equal or exceed developmental disorders like Autism Spectrum Disorder (CDC, 2014). Importantly, prevalence estimates for FAS have essentially remained unchanged since the syndrome was first defined (Jones et al., 1973; Lemoine et al., 1968), while estimates for FASD appear to be increasing. Moreover, fetal alcohol exposure contributes to the emergence of secondary mental health disabilities (O'Connor and Paley, 2009). FASD is over-represented in foster care, juvenile justice and adult prison populations (Ospina and Dennett, 2013), and is a public health and economic burden (Popova et al., 2012). It seems reasonable to ask why FASD cannot be prevented. Several social cultural and biological factors contribute to this resistance to elimination.

2. **FASD is difficult to prevent:** FASD is often presented as a ‘completely preventable’ disorder. The prevailing opinion is that if women simply did not drink during pregnancy, then FASD would cease to exist. However, sociocultural factors that contribute to the prevalence of unplanned pregnancies and to alcohol consumption make such a scenario unlikely. Firstly, in the US as an example, a majority of pregnancies are unplanned (Finer and Zolna, 2014). Sex education programs in the US public education system, that focus entirely on abstinence (Stanger-Hall and Hall, 2011), and limited utilization of contraception among young women (CDC, 2013) may contribute to a high rate of teen pregnancies and to the overall prevalence of unplanned pregnancies. Moreover, several psychosocial and physiological factors can delay awareness of pregnancy and may even result in denial of pregnancy (Brezinka et al., 1994; Wessel et al., 2002). Therefore, despite published prevention guidelines from the American Congress of Obstetricians and Gynecologists (ACOG, 2011), **women with unanticipated pregnancies may inadvertently expose their fetus to alcohol.** Moreover, women with alcohol use disorders can experience aversive withdrawal symptoms due to addiction, which makes it difficult to curtail alcohol consumption during pregnancy. Not surprisingly, a 2013 report by the Substance Abuse and Mental Health Services Administration (SAMHSA) found that ~18% of US women consumed alcohol during early pregnancy, and 6.6% of women reported binge-drinking episodes (SAMHSA, 2013), a pattern of drinking that is particularly damaging to fetal development (Bonthius and West, 1990).

Though the NIAAA defines a binge episode as the consumption of at least four standard drinks at one time for women, actual consumption levels are likely to be higher. According to a recent report by the Centers for Disease Control and Prevention (CDC), on average, US women report consuming ~6 drinks per binge episode (CDC, 2012), resulting in peak blood alcohol concentrations (BACs) that may exceed 270mg/dl (TABC, 2014). Though the SAMHSA report found that self-reported drinking declined substantially through pregnancy, other empirical assessments suggest otherwise. For example, a 2013 study of births in a New Mexico hospital found that 6.5% of newborn infants screened positive for the alcohol metabolite phosphatidyl-ethanol at

[www.nofas-uk.org](http://www.nofas-uk.org)
levels, indicative of definitive alcohol exposure in late pregnancy (Bakhireva et al., 2013). These data suggest that alcohol consumption during pregnancy will be difficult to eliminate.

Finally, a focus on the alcohol consumption behavior of the pregnant mother to the exclusion of other sources of fetal damage due to alcohol exposure is likely to be misplaced. For example, paternal alcohol consumption may be a significant and largely unacknowledged contributory factor to FASD, resulting in growth, neurobiological and behavioral deficits in offspring (reviewed in (Finegersh et al., 2015)). Moreover, effects of fetal alcohol exposure may be passed from one generation to the next (reviewed in (Mead and Sarkar, 2014)), suggesting that a multi-generational family history of alcohol consumption may be a contributory factor in FASD. The converging trends of unplanned pregnancies, preconception paternal alcohol consumption, binge patterns of alcohol consumption, and multigenerational histories of exposure mean that FASD is difficult to prevent by education alone. These factors also emphasize a clear need for biomarkers that facilitate early diagnosis of FASD, and particularly, for biomarkers that predict the effects of fetal alcohol exposure.

3. Biomarker development: It is clear that an early diagnosis would facilitate early intervention that in turn may mitigate disabilities that emerge later in life (Hellemans et al., 2010). Several promising biomarkers for fetal alcohol exposure have been identified, including fatty acid ethyl ester in neonatal meconium (Bearer et al., 2005; Peterson et al., 2008), ethyl glucuronide in placenta (Matlow et al., 2012), and phosphatidylethanol in newborn blood (Bakhireva et al., 2013). All of these biomarkers are promising, and have been successfully to detect exposure. However, these are markers for exposure and do not predict effect. Here we will discuss the potential use of a novel class of small endocrine RNA molecules, microRNAs (miRNAs) that are secreted into the vascular system of humans and animals as biomarkers that predict ‘effect’.

4. MicroRNAs (miRNAs) as Biomarkers for FASD: MiRNAs are a class of small non-protein-coding RNAs that, among several functions, serve as intracellular negative regulators of protein translation (Miranda, 2012). The human genome encodes ~2500 miRNAs (Griffiths-Jones et al., 2008). These small RNAs are generally transcribed as apart of a much longer transcript, termed a primary-miRNA (pri-miRNA). Sequential processing of the pri-miRNA first within the nucleus and then in the cytoplasm, results in the biogenesis of a small RNA fragment of 17-25 nucleotides in length (Lee et al., 2002). Mature miRNAs are loaded onto a complex of proteins collectively called the RNA induced-silencing complex (RISC). RISC/miRNA complexes bind to the 3’-untranslated region of (protein coding) mRNAs to silence protein translation. Single miRNAs can bind to the 3’UTRs of multiple protein-coding genes to suppress the activity of gene networks that are important for cell renewal, maturation and even death (for review, see (Miranda, 2014)).

We first showed that miRNAs were sensitive to alcohol (Sathyan et al., 2007) and that alterations in these miRNAs mediated effects of alcohol on neural stem cell proliferation (Sathyan et al., 2007) and maturation (Tsai et al., 2014), and cranial development (Pappalardo-Carter et al., 2013) in animal models. A growing body of evidence has since shown that miRNAs play an important role in alcohol addiction and toxicity. For example, acute ethanol tolerance (Pietrzykowski et al., 2008), intermittent exposure and withdrawal (Guo et al., 2012; Steenwyk et al., 2013), chronic alcoholism in human (Lewohl et al., 2011) and in animal models (Tapocik et al., 2013), and neurotoxicity (Yadav et al., 2011) result in altered miRNA expression and function. Outside the brain, alcohol exposure also alters miRNA expression and function associated with gut leakiness and liver damage (Tang et al., 2008), steatohepatitis (Dolganiuc et al., 2009), inflammation (Bala and Szabo, 2012), fibrosis (Meng et al., 2012), and bone remodeling (Sampson et al., 2011).
5. Plasma miRNAs are a novel class of blood-borne biomarkers: In 2008, evidence emerged that miRNAs were secreted into plasma (Hunter et al., 2008) and could mark the presence of fetal trisomy (Go et al., 2008), identify patients with prostate cancer (Mitchell et al., 2008). We therefore assessed in an animal model whether plasma miRNAs in the pregnant mother and newborn infant could serve as a marker for fetal alcohol exposure (Balaraman et al., 2014). In this sheep model of gestational binge alcohol exposure, pregnant ewes were assigned to alcohol and control groups, for a period analogous to the three trimesters of a human pregnancy (Ramadoss et al., 2007). Pregnant sheep were subjected to a weekly regimen of three days of binge exposure followed by a four-day rest period. The binge exposure resulted in a peak blood alcohol concentration of 243.2±20.3 mg/dl (0.24mg/%) or three time the legal limit for intoxication in the US). Blood was drawn from the ewe at 24 hr following the final episode of ethanol exposure and from the lamb within 1 hr of birth. We assessed the expression of 750 miRNAs in maternal and infant plasma. Data were subjected to analysis of variance with a Benjamini and Hochberg correction for multiple comparisons (α=0.05). Plasma miRNAs that passed criterion (55 or 7.3% of the sampled miRNAs) were subjected to principal component analysis (PCA). This analysis identified a group of plasma miRNAs (PCA(component-1), Figure 1A, data extracted from (Balaraman et al., 2014)) whose changes in expression discriminated between the alcohol exposed infant and all other groups including the alcohol-exposed pregnant mother. These data suggest that plasma miRNAs in the infant could be a biomarker for fetal alcohol exposure. However, are they also a biomarker for fetal alcohol effect?

6. MiRNAs as biomarkers of the effect of fetal alcohol exposure: The case of mir-9. One of several miRNAs that discriminated between controls and lambs that were prenatally exposed to alcohol was mir-9 (Figure 1B). We found that mir-9 was expressed at lower levels in plasma of alcohol-exposed newborn lambs compared with controls, but that this miRNA was expressed at higher levels in the plasma of the alcohol exposed pregnant mother (Balaraman et al., 2014). MiR-9 is highly expressed in the developing fetal brain and has been shown to play a critical role in organizing brain development (Leuchtt et al., 2008) and in promoting the maturation of neural stem cells into neurons (Delaloy et al., 2010; Shibata et al., 2008; Shibata et al., 2011). Plasma miR-9 may originate from brain and consequently, reflect changes in brain miR-9. In support of this hypothesis, we (Balaraman et al., 2012; Pappalardo-Carter et al., 2013; Sathyan et al., 2007) and other research groups (Tal et al., 2012) have observed that early developmental alcohol exposure results in a significant loss of miR-9 in developing neural tissues. Specifically, in a zebrafish model, we found that embryonic exposure to alcohol resulted in decreased miR-9 expression that was associated with microcephaly (Figure 2). Importantly, knocking down expression of miR-9 in the zebrafish embryo also resulted in microcephaly (Figure 3) as well as behavioral deficits similar to those observed following alcohol exposure. Thus miR-9 may mediate some of alcohol’s effects on fetal development.

In conclusion, FASD is difficult to prevent, particularly since the alcohol consumption pattern of the mother may only be one contributory factor, and the effects of paternal alcohol consumption and trans-generational transmission of FASD are largely ignored. FASD is also difficult to diagnose since many fetal alcohol-affected infants and children do not exhibit characteristic growth and mid-face hypo-development deficits. This means that many un-diagnosed FASD children are at risk for developing secondary disabilities. There is a real need for biomarkers that are not only sensitive to exposure, but also predict effect. Plasma miRNAs, like miR-9, are not only examples of biomarkers for fetal alcohol exposure, but that the expression level of mir-9 and other plasma miRNAs may predict neuro-developmental and other disabilities due to fetal alcohol exposure. These plasma miRNAs represent a novel class of endocrine factors. Profiling the expression of these novel endocrine molecules may provide new insights into disease diagnosis, etiology and treatment.

www.nofas-uk.org
Figure 1: Plasma microRNA biomarkers for maternal and fetal alcohol exposure in an Ovine model (data adapted from (Balaraman et al., 2014)). In utero, maternal three trimester-equivalent exposure to binge episodes of alcohol results in significant changes in plasma miRNA profiles in the dam and persistent changes in plasma miRNA profiles in the neonatal lamb. (A) Principal components analysis (PCA), component 1 (Comp1) separates the neonatal lamb exposed in utero to alcohol from all other groups, whereas principal component 2 (Comp2) separates the alcohol-exposed pregnant dam from both control pregnant dam and control neonatal lamb. Each blue dot represents a miRNA that passed Benjamini and Hochberg-corrected analysis of variance, at a p<0.05. Data for microRNA, miR-9 (encircled in green), is presented as a histogram in panel ‘B’. (B) Mir-9 expression was significantly increased in plasma from the alcohol-exposed dam compared to control, but significantly decreased in plasma from neonatal lamb compared to control.
**Figure 2:** Alcohol exposure in a zebrafish model (data adapted from (Pappalardo-Carter et al., 2013)).

**(A)** Control zebrafish exhibit a well-developed head and brain expression of miR-9 (blue colored hybridization product, delineated by red arrows) at 48 hours post-fertilization. **(B,C)** Exposure of the early embryo (morula stage) to alcohol results in a loss of miR-9 expression (loss of blue hybridization product) accompanied by diminished head size (microcephaly).
Figure 3: MiR-9 knockdown results in microcephaly (data adapted from (Pappalardo-Carter et al., 2013)).

(A,B) Control embryos and embryos injected with a nonsense control reagent proceed to develop normally and exhibited well-developed heads at 24 hours post-fertilization (circled). (C) Embryo injected with an anti-miR-9, antisense morpholino to knockdown miR-9 expression, exhibited a loss of cranial tissue at 24 hours post-fertilization (circled) indicative of microcephaly, an effect similar to that produced by alcohol exposure.

References:


Back to Table of Contents
Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE): An Area for Further Consideration

Jerrod Brown, Adam Piccolino, Judge Anthony Wartnik, Tina Andrews, Mary Weaver, Anne Russell, Hannah Brown and Megan Lea

Jerrod Brown MA, MS, MS, MS, is the treatment director for Pathways Counseling Center, Inc. Jerrod is also the founder and CEO of the American Institute for the Advancement of Forensic Studies (AIAFS).

Hannah Brown, is a volunteer mental health research assistant with the American Institute for the Advancement of Forensic Studies (AIAFS). She will graduate from Macalester College in 2015 with a Bachelor of Arts degree in Neuroscience.

Adam L Piccolino, PsyD, ABN, is a board-certified neuropsychologist with over 18 years of providing direct clinical services in corrections. Dr. Piccolino has lectured locally and nationally on a variety of topics including the identification and management of traumatic brain injury, dementia, and other neurocognitive disorders within an offender population.

Judge Anthony P. (Tony) Wartnik, served as a trial judge for 34 years, nine of which were on the Bellevue District Court, a limited jurisdiction court and almost 25 years on the King County, Washington Superior Court, a general jurisdiction court. In the latter capacity, he presided over involuntary mental illness treatment commitment cases, juvenile offender and dependency cases, adult criminal cases, and family law cases in addition to other assigned responsibilities. He chaired a task force in the mid-1990s to establish protocols in Juvenile Court for determining the competency of youth with organic brain damage and chaired the Governor’s Advisory Panel of Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE). Since retirement from the court in 2005, Tony has served as a consultant to the Fetal Alcohol and Drug Unit, University of Washington, School of Medicine and as the Legal Director/Liaison for FASD Experts, a multidisciplinary Forensic Assessment and Diagnostic Team.

Tina Andrews, MBA, MEd, is co-founder and member of the Board of Directors for Families Affected by FASD. FAFASD works to raise awareness through education, support, and research-based training for family and professionals working with individuals with an FASD. Tina is also the author of a blog, Ten Second Kids in a Two Second World, where she explores a wide range of topics related to being a caregiver for a child with FASD. Ms. Andrews works full time in quality and statistical analysis in addition to her FASD advocacy efforts.

Mary Mahoney Weaver, has a Bachelor of Science degree in Human Services and is the Northwest Prevention Initiatives Coordinator for Minnesota Communities Caring for Children/Prevent Child Abuse Minnesota and contracts with Minnesota Organization on Fetal Alcohol Syndrome for family support work. She is a public member of the Minnesota Board of Social Work, appointed by
Anne Russell, is the biological mother of two adult children with Fetal Alcohol Spectrum Disorder (FASD). Since 2000, Anne has worked to raise awareness in Australia pertaining to alcohol and pregnancy and FASD. In 2005, she published the first of three books and is currently preparing the second edition of Alcohol and Pregnancy – My Responsible Disturbance. In 2007, she founded the Russell Family Fetal Alcohol Disorders Association (RFFADA) which provides support for over 200 parents around the world.

Megan Lea, BA, is a graduate of the College of Saint Benedict and Saint John’s University in Sociology. Ms. Lea will graduate from Saint Mary’s University Twin Cities in 2015 with a Master’s Degree in Counseling and Psychological Services. Megan is currently completing her Practicum at Pathways Counseling Services, Inc. working with individuals impacted by mental illness.

The purpose of this article is to summarize the proposed guidelines for the Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE) diagnosis found in the “Further Study” section of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) and to examine some implications of its inclusion. Along with other disorders related to prenatal alcohol exposure, the prevalence of ND-PAE is estimated to be between 2 percent and 5 percent in the United States (American Psychiatric Association, 2013). Prior to the DSM-5, there was not a mental health-related diagnosis to address and describe prenatal exposure to alcohol. In fact, prenatal exposure to alcohol was treated as an Axis III medical condition that only a medical professional could diagnose with very specific information. However, a multi-disciplinary approach was developed over time, which required a medical doctor to make an official medical diagnosis and a mental health professional (other than psychiatrists) to identify the mental health features of Fetal Alcohol Spectrum Disorder (FASD). The mental health professional assessment identified the lifelong/lifespan impairments related to the FASD diagnosis, as well as providing a forensic (issues related to the law and the legal system) prognosis when warranted.

With the publication of the DSM-5, a mental health diagnosis of prenatal exposure no longer requires a medical professional. If an individual has symptoms of a neurodevelopmental disorder resulting in impaired social, occupational, or educational functioning, but does not meet the criteria of another neurodevelopmental disorder currently listed in the DSM-5 (e.g., Autism), then a mental health professional may assign a diagnosis of “Other Specified Neurodevelopmental Disorder.” Further, if it is confirmed (or suspected and/or supported by collateral reporting) that this neurodevelopmental condition is related to prenatal exposure to alcohol, the mental health professional may add a specifier of “Associated with Prenatal Alcohol Exposure.” Therefore, a diagnosis of “Other Specific Neurodevelopmental Disorder (Associated with Prenatal Exposure to Alcohol)” can be provided when appropriate.

Proposed Diagnosis:

As it is currently classified in the DSM 5, “Other Specified Neurodevelopmental Disorder (Associated with Prenatal Exposure to Alcohol)” can include FASD, but this diagnosis can include other neurological disorders as well. In the “Further Study” section of the DSM-5, a proposed diagnosis directly associated with FASD, “Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE)” is suggested. This proposed disorder is directly associated with prenatal alcohol exposure that often results in cognitive, regulatory, and adaptive impairments manifested in early childhood and persist throughout an individual’s lifespan. Cognitive impairments associated with ND-PAE may include low IQ, diminished executive functioning, learning disabilities, memory difficulties, and visuospatial reasoning problems. Regulatory impairments associated with ND-PAE may include mood and aggression problems, attention deficits, and impulsivity. Adaptive
impairments associated with a potential ND-PAE diagnosis must include verbal communication and/or social interaction complications. Additional impairments in adaptive functioning may also include compromised daily living skills and deficits in motor skills. The diagnosis of ND-PAE does not require all listed symptoms to be present.

Each individual impacted by prenatal exposure to alcohol may present with a unique combination of impairments based on individual genetic and epigenetic makeup, the pattern of prenatal alcohol exposure experienced, and/or other environmental factors. Unlike some of the medical diagnoses related to FASD, ND-PAE can be diagnosed regardless of whether facial dysmorphology or other visible physical effects of prenatal alcohol exposure are present. The commonly known observable manifestations of FASD, such as facial dysmorphology (thin upper lip and absent philtrum), shortened eye openings, flattened mid face, small physical stature, and small head circumference, are not universal. Research has found children who are exposed to alcohol during pregnancy can have abnormal brain anatomy and chemistry whether or not facial dysmorphology is present (Cortese et al., 2006). The damage to the unborn child caused by prenatal alcohol exposure depends on the developmental stage of the fetus at the time of exposure. Brain and central nervous system damage is the most common persisting sequelae because these systems begin developing early and continue throughout pregnancy and after birth.

Comorbidity:

To be diagnosed with the proposed ND-PAE diagnosis, it must be clear those presenting symptoms characteristic of the disorder were caused by exposure to alcohol during the pregnancy. That is, the symptoms cannot be explained by postnatal alcohol or drug use, any general medical condition, the impact of other teratogens, genetic disorders, and/or environmental neglect. It is important to note the ND-PAE diagnostic criteria specifically allows for collateral reporting (i.e., reporting by persons other than the mother) of alcohol consumption during the pregnancy. This is a significant departure from previous diagnostic criteria related to FASD requiring the mother’s admission of alcohol consumption during the pregnancy.

Even with the emphasis on ruling out other potential causes of the symptoms characteristic to ND-PAE, over 90% of those diagnosed with ND-PAE will have a co-occurring diagnosis. The most common are: Attention-Deficit/Hyperactivity Disorder (ADHD), Oppositional-Defiant Disorder (ODD), Conduct Disorder (CD), bipolar-related disorders, mood disorders, and/or substance abuse (Barr et al., 2006; Mattson, Crocker, & Nguyen, 2011; O’Connor et al., 2002; Walthall, O’Connor, & Paley, 2008). Secondary symptoms related to unrecognized FASD/ND-PAE (i.e., low IQ, executive functioning, learning, and memory) are often diagnosed separate from the alcohol-related deficits (Streissguth, 1997). As such, secondary diagnostic symptoms must be evaluated carefully to determine if there is indeed a comorbid condition or if these impairments are a function of the underlying ND-PAE. The appropriateness and effectiveness of various interventions may vary widely depending on the cause of observed symptoms.

The cognitive, regulatory, and adaptive impairments associated with prenatal exposure to alcohol may be difficult to measure during infancy; therefore, mental health professionals may wish to defer any formal diagnosis until the pre-school or school years. However, careful consideration should be given in weighing the risks of an inaccurate diagnosis with the known benefits of early intervention. Intervention strategies for ND-PAE (i.e., early development and learning programs, sensory integration therapies, speech and language therapies, etc.) are not invasive and if initiated based on an inaccurate diagnosis, are unlikely to negatively impact children.

Prognosis:

The impairments associated with the proposed ND-PAE diagnosis can hinder an affected individual from interacting with established social systems to achieve expected adult milestones and therefore, a successful and enriching life. These individuals are more likely to experience problems with school, unemployment, the criminal justice system, involuntary legal or psychiatric commitment, living independently, and/or suicide (Astley & Clarren, 2000; Church, Eldis, Blakley, & Bawle, 1997; Fast & Conry,
Within the justice setting, these impairments may affect an individual’s ability to understand *Miranda* rights, reliability of testimony, and fitness to stand trial. With the development of the DSM-5, Mental Retardation has been redefined as Intellectual Disability (Intellectual Developmental Disorder) (ID) and puts adaptive behavioral deficits (present with ND-PAE) on equal footing with full scale IQ. It also eliminates the previous hard-line approach of a strict full scale IQ standard of 69 or below which has been previously required to diagnose an intellectual disability. The U.S. Supreme Court, in the case of *Hall v. Florida* (2014), adopted the DSM-5 definition of ID. This ruling, which revisited and re-affirmed the case of *Atkins v. Virginia* (2002), prohibits a person diagnosed with ID, who is convicted of a capital or death penalty offense, to be put to death. Prior to *Atkins v. Virginia* (2002) and *Hall v. Florida* (2014), a person with ID is exempt from the imposition of the death penalty. The adaptive behavioral deficits identified by the Supreme Court in these cases are, by and large, the very same deficits that constitute the neurobehavioral criteria of ND-PAE. Given these implications, law enforcement (e.g., police officers, sheriffs, and detectives); criminal justice (e.g., wardens, correctional guards, and probation officers); and legal professionals (e.g., attorneys and judges) should be educated about the signs and symptoms of ND-PAE. Such education would increase their ability to work constructively with individuals diagnosed with ND-PAE, resulting in treatment more consistent with evolving case law and the requirements of the Americans with Disabilities Act.

In an educational setting, the impairments associated with ND-PAE make it highly unlikely an affected individual would experience success without special supports. ND-PAE may go unrecognized when using standard screenings to determine the need for special education services because, as discussed, it is possible for a person to experience substantial adaptive and regulatory deficits while still exhibiting adequate intellectual functioning. If a student goes undiagnosed and/or appropriate support is not provided, then the right to a free and appropriate public education (FAPE) guaranteed by the Individuals with Disabilities Education Act (IDEA) is not fulfilled. Aside from individual rights issues, an interrupted or incomplete education further increases the likelihood of unemployment, homelessness, substance abuse, and involvement in the justice system. There is evidence the development of these adverse outcomes can be significantly mitigated by certain protective factors, in particular early diagnosis and intervention. Appropriate accommodations and supports can also help prevent adverse outcomes.

**Conclusion:**

Training education professionals in the signs and symptoms of ND-PAE, as well as constructive methods to engage and teach affected persons, would be of tremendous social benefit. Moreover, social workers, substance abuse treatment professionals, foster parents, prospective adoptive parents, and a host of other helping professionals, who are also highly likely to come into contact with persons who have ND-PAE, would also benefit from training. Inclusion of ND-PAE in the “Further Study” section of the DSM-5 and the ability to currently diagnose using “Other Specific Neurodevelopmental Disorder (Associated with Prenatal Exposure to Alcohol)” will hopefully increase the recognition and support for affected parents and children as they interact with social services, treatment professionals, counselors, and the educational/justice systems.

It should be noted there are some concerns regarding the inclusion of ND-PAE in the DSM-5. Since prenatal exposure to alcohol causes a wide range of structural, functional, and neurological problems, it has been posited a medical, rather than mental health, diagnosis is more accurate and
thus more appropriate. While in theory, considering a physical disability as a mental health
diagnosis may be inaccurate, in practice, many persons affected by FASD, especially those lacking
physical dysmorphism, enter the mental health system due to behavioral symptoms and comorbid disorders. The lack of an official mental health diagnosis covering the many unique
presentations of FASD has left it very much an “invisible disability.” Therefore, further research of
ND-PAE as a neurobehavioral and/or neurodevelopmental disorder will allow for better prevalence
estimates, development of standardized identification and treatment protocols, and effective social
policy to ameliorate this preventable health condition. In addition to research, a concerted effort to
raise awareness to the unique challenges of those impacted by prenatal exposure to alcohol,
related public policy, and specific education to professionals in all likely fields of contact, are highly
recommended.

References


1. **Diagnosing FASD in Adults: The Development and Operation of an Adult FASD Clinic in Ontario, Canada**
   Valerie K. Temple, Jillian Ives, Ann Lindsay
   Corresponding Author: Valerie.Temple@surreyplace.on.ca

   **ABSTRACT**
   This paper describes the development and operation of an interdisciplinary Fetal Alcohol Spectrum Disorders (FASD) diagnostic clinic focusing specifically on adults. The clinic is embedded within a community-based interdisciplinary health agency specializing in intellectual and developmental disabilities. A review of the clinic’s assessment process is presented describing the steps from intake to feedback and intervention. To date, the clinic has received 93 referrals and given 41 alcohol-related diagnoses including 10 completed using videoconferencing technology. Issues unique to adult diagnosis are discussed as well as some of the challenges, including high rates of cancellations/no-shows for appointments, obtaining background and historical information, establishing maternal alcohol history, working collaboratively with other support sectors such as children’s protective services and the justice system, and finding appropriate follow-up and intervention services in the community. Recommendations for future work to support adults with FASD and their families are presented.

   Read Full Article
   [Link](http://www.jptcp.com/pubmed.php?articleId=509)

   Back to Table of Contents

   Jak Ozsarfat, Gideon Koren
   Corresponding Author: gkoren@sickkids.ca

   **ABSTRACT**
   The majority of children with FASD suffer from disruptive behaviors and most of them need medications to modify these behaviors. The objective of this review is to familiarize professionals caring for children with FASD with stimulants and other drugs for ADHD, and the second generation antipsychotic risperidone - for aggressive and defiant behaviors.

   Read Full Article
   [Link](http://www.jptcp.com/pubmed.php?articleId=505)

   Back to Table of Contents

3. **Investigating the Fetal and Postnatal Effects of Paternal Alcohol Exposure in Mouse Offspring: A Review**
   Marta Baber, Gideon Koren (Canada); gkoren@sickkids.ca

   Read Full Article
   [Link](http://www.jptcp.com/pubmed.php?articleId=507)

   Back to Table of Contents
ABSTRACT
To further elucidate the possible effects of paternal alcohol exposure on fetal and post-natal development, Lee et al. conducted an experimental animal study from which potential transgenerational consequences of paternal alcohol exposure on mouse offspring were explored. The authors concluded that paternal alcohol consumption likely poses some risk to those developing offspring.

However, the authors’ analysis of the incidence of fetal abnormalities may be misleading. The incidence of abnormality for each treatment group was calculated by dividing the number of abnormalities by the total number of dames. This approach to presenting the data is misrepresentative, because if a dame were carrying one abnormally developed fetus out of a litter of, say, 16, the entire litter would be captured as an “abnormality” in the calculation of incidence.

Read Full Article, http://www.jptcp.com/pubmed.php?articleId=504

Back to Table of Contents


4. Anticipatory Guidance to Children and Adolescents with Fetal Alcohol Spectrum Disorder (FASD): Practice Points for Primary Health Care Providers
   Ana Hanlon-Dearman, Courtney R. Green, Gail Andrew, Nicole LeBlanc, Jocelynn L. Cook
   Corresponding Author: ahdearman@hsc.mb.ca

ABSTRACT
Background
Fetal Alcohol Spectrum Disorder (FASD) is an umbrella term that describes the range of effects that can occur in an individual who was prenatally exposed to alcohol and includes an array of complex neurodevelopmental and physical findings.

Objectives
To give primary healthcare providers (PHCP) evidence-based recommendations for supporting and managing the symptoms of FASD after patients have received a diagnosis.

Methods
Primary health recommendations for the management of children and adolescents with FASD were developed based on expert clinical judgment and supported by evidence-based research, where appropriate. The format was adapted from other health supervision practice guidelines as developed by the American Academy of Pediatrics. Clinical practice “Points” for the PHCP are highlighted. A reference table of anticipatory recommendations by age is presented.

Results
In most cases, the initial screening and referral for diagnosis will be made by the PHCP, and they will be responsible for ongoing management. It is anticipated that these recommendations will provide the PHCP with evidence to support the longitudinal health care of children and adolescents with FASD and their families as they transition throughout all developmental stages.

Conclusion
There is a pressing need for the involvement of PHCP in the active care of children and adolescents with FASD and their families over the lifespan. PHCP are trained in screening, prevention, and management of health needs, and are in the position to coordinate sub-specialty referrals as needed. Engaging PHCP will provide a truly integrated care system for individuals with FASD and their families.
5. The Cost of Lost Productivity Due to Fetal Alcohol Spectrum Disorder-Related Premature Mortality
Brian Easton, Larry Burd, Anna Sarnocinska-Hart, Jürgem Rehm, Svetlana Popova
Corresponding Author: lana.popova@camh.ca

ABSTRACT

Background
Individuals with Fetal Alcohol Spectrum Disorder (FASD) have increased mortality as compared to the general population.

Objectives
To estimate the productivity losses due to premature mortality of individuals with FASD in Canada in 2011.

Methods
A demographic approach with a counterfactual scenario in which nobody in Canada is born with FASD was used. Population estimates were calculated using data on the labour force, unemployment rate, and average weekly wage obtained from Statistics Canada. The number of FASD-related deaths, coded in the International Classification of Diseases, version 10, was estimated based on data from Statistics Canada and pooled prevalence estimates of the major disease conditions associated with FASD were obtained from a meta-analysis. The estimates of FASD-related mortality rates served as a basis for the length of working life span estimation. Once the number of working years lost to premature deaths was derived, productivity losses were computed.

Results
It was estimated that in total 327 individuals with FASD aged 20 to 69 (almost twice as many men as women) died in Canada in 2011. As a result, there were 2,877 years of potential employment lost, which translated to a loss ranging from $88 million to $126 million. This amount represents the increase in national income, had there been no premature mortality from FASD and the workers with FASD had been typical members of the labour force (without compromised productivity due to FASD).

Conclusions
The estimates of productivity losses further reinforce the value of FASD prevention as a primary strategy.

Susan J. Astley
ABSTRACT

Background

Accurate fetal alcohol spectrum disorder diagnoses require accurate facial measurement. The Fetal Alcohol Syndrome (FAS) Facial Photographic Analysis Software was developed to overcome measurement error known to occur with ruler measurement of the PFL. Recent publications have queried the Software’s accuracy.

Objectives

1) Demonstrate the Software’s ability to accurately measure a PFL from a 2-dimensional digital facial photograph.

2) Demonstrate the frequency and magnitude of error when the PFL is measured directly by clinicians using a ruler.

Methods

Objective 1: PFLs of mannequins were measured using the Software and a sliding digital caliper, with the latter serving as the gold-standard accurate measure. Mannequins allowed the caliper prongs to be placed directly on the landmarks that define the PFL. Objective 2: PFLs of 1,027 patients evaluated at the University of Washington FAS Diagnostic & Prevention Network were measured with the Software and directly by one or two clinicians using a ruler.

Results

Objective 1: The Software derived PFLs that were identical to or within 0.2 mm of the caliper measures. Objective 2: There was tremendous inter-rater variability in PFLs measured by clinicians using a hand held ruler. Seventy-seven percent of patients had their PFLs measured incorrectly (greater than 1 mm error) by at least one of the two clinicians using a ruler.

Conclusion

The FAS Facial Photographic Analysis Software measures the PFL with the same accuracy as a sliding digital caliper, as it was programmed to do. Direct measurement of the PFL with a ruler is very prone to error.

Read Full Article

http://www.jpctp.com/pubmed.php?articleId=500

Back to Table of Contents


7. Associations between late and moderately preterm birth and smoking, alcohol, drug use and diet: a population-based case-cohort study

Smith LK, Draper ES, Evans TA, Field DJ, Johnson SJ, Manktelow BN, Seaton SE, Marlow N, Petrou S, Boyle EM (UK)

ABSTRACT

OBJECTIVE:

This study explores the associations between lifestyle factors and late and moderate preterm birth (LMPT: 32+0-36+6 weeks’ gestation), a relatively under-researched group.

STUDY DESIGN:

A population-based case-cohort study was undertaken involving 922 LMPT and 965 term (37+ weeks’ gestation) singleton live and stillbirths born between 1 September 2009 and 31 December
Women who smoked during pregnancy were at 38% increased risk of LMPT birth compared with non-smokers (RR 1.38, 95% CI (1.04 to 1.84)). Low consumption of fruit and vegetables was associated with a 31% increased risk compared with those who reported eating higher consumption levels (RR 1.31 (1.03 to 1.66)). Women who did not have any aspects of a Mediterranean diet were nearly twice as likely to deliver LMPT compared with those whose diet included more Mediterranean characteristics (RR 1.81 (1.04 to 3.14)). Women who smoked and consumed low levels of fruit and vegetables (5% of women) were at particularly high risk (RR=1.81 (1.29 to 2.55)). There was no significant effect of alcohol or recreational drug use on LMPT birth.

CONCLUSIONS:
Smoking and poor diet during pregnancy, factors that strongly impact on very preterm birth, are also important at later gestations and experienced together are associated with an elevated rate of risk. Our findings suggest early cessation of smoking during pregnancy may be an effective strategy to reduce LMPT births.

8. Voluntary Exercise Partially Reverses Neonatal Alcohol-Induced Deficits in mPFC Layer II/III Dendritic Morphology of Male Adolescent Rats
Hamilton GF, Criss KJ, Klintsova AY (USA)

ABSTRACT
Developmental alcohol exposure in humans can produce a wide range of deficits collectively referred to as Fetal Alcohol Spectrum Disorders (FASD). FASD-related impairments in executive functioning later in life suggest long-term damage to the prefrontal cortex (PFC). In rodent neonates, moderate to high levels of alcohol exposure decreased frontal lobe brain size and altered medial PFC pyramidal neuron dendritic morphology. Previous research in our lab demonstrated that neonatal alcohol exposure decreased basilar dendritic complexity but did not affect spine density in Layer II/III pyramidal neurons in 26-30 day old rats. The current study adds to the literature by evaluating the effect of neonatal alcohol exposure on mPFC Layer II/III basilar dendritic morphology in adolescent male rats. Additionally, it examines the potential for voluntary exercise to mitigate alcohol-induced deficits on mPFC dendritic complexity. An animal model of binge drinking during the third trimester of pregnancy was used. Rats were intubated withalcohol (alcohol-exposed, AE; 5.25g/kg/day) on postnatal day (PD) 4-9; two control groups were included (suckle control and sham-intubated). Rats were anesthetized and perfused with heparinized saline solution on PD 42, and brains were processed for Golgi-Cox staining. Developmental alcohol exposure decreased spine density and dendritic complexity of basilar dendrites of Layer II/III neurons in the medial PFC (mPFC) compared to dendrites of control animals. Voluntary exercise increased spine density and dendritic length in AE animals resulting in elimination of the differences between AE and SH rats. Thus, voluntary exercise during early adolescence selectively rescued alcohol-induced morphological deficits in the mPFC.
9. **Prevalence of Fetal Alcohol Syndrome in a South African City with a Predominantly Black African Population**

Urban MF, Olivier L, Viljoen D, Lombard C, Louw JG, Drotsky LM, Temmerman M, Chersich MF (South Africa)

**ABSTRACT**

**BACKGROUND:**
Fetal alcohol spectrum disorder (FASD) and fetal alcohol syndrome (FAS) are common in some South African populations, notably those of mixed ancestry descent in rural areas and small towns. Little is known about FAS/FASD prevalence in the majority of South Africans: city dwellers of Black African ethnicity. This study describes the prevalence of FAS in a South African city, comparing 2 suburbs with predominantly mixed ancestry (Roodepan) and Black African (Galeshewe) populations that house over 60% of the city population.

**METHODS:**
We conducted a tiered, active case ascertainment study for the prevalence of FAS and also detected some less clinically specific FASD cases. All first-grade learners in the 2 suburbs were eligible for anthropometric screening, and screen-positive learners were assessed for dysmorphic features of FAS. Those with suggestive clinical features received neurocognitive assessment, and maternal or collateral interview. Final diagnosis was made following a case conference.

**RESULTS:**
Complete ascertainment of FAS status was made in 1,503 (94.7%) of 1,587 eligible learners (435 in Roodepan and 1,152 in Galeshewe). Overall, FAS was diagnosed in 83 (5.5%, 95% confidence interval [CI] = 4.4 to 6.8) learners and FASD in 96 (6.4%, 95% CI = 5.2 to 7.7). Levels of FAS were high in both areas: 26 (6.3%, 95% CI = 4.2 to 9.2) learners from Roodepan, compared to 57 (5.2%, 95% CI = 4.0 to 6.7) from Galeshewe (p = 0.39). No cases were previously diagnosed. The mortality rate for mothers of FASD children from Galeshewe was 19 of 65 (29%), compared to 3 of 31 (9.7%; p = 0.03) for Roodepan. Interviewed mothers in Galeshewe were older and had higher body mass index.

**CONCLUSIONS:**
Prevalence of FAS is high in both Galeshewe and Roodepan, and the lack of prior diagnoses indicates that awareness remains low. The maternal mortality rate was especially high in Galeshewe. The unexpectedly high burden of FAS in an urban area with predominantly Black African population mandates extension of surveillance and intervention measures in southern Africa.

Read Full Article

**10. Determination of direct alcohol markers: a review**

Cabarcos P, Álvarez I, Tabernero MJ, Bermejo AM.; (Spain)

**ABSTRACT**
Alcohol is the most popular legal drug used in our society today, and its consumption by pregnant women remains an important public health problem. Gestational alcohol consumption can result in a continuum of adverse fetal outcomes known as fetal alcohol spectrum disorder (FASD). Effective strategies are needed to prevent the increasing adoption of risky drinking behaviors.
Because ethanol itself is only measurable for a few hours after ethanol intake in conventional matrices including blood, urine, and sweat, these matrices are only useful to detect recent ethanol exposure. Since approximately early 2000, the non-oxidative ethanol metabolites have received increasing attention because of their specificity and, in some cases, wide time window of detection in non-conventional matrices including hair and meconium. In the attempt to update analytical methods for the determination of non-oxidative markers of alcohol, the objective of this study is to review published studies that measure fatty-acid ethyl esters (FAEE), ethyl glucuronide (EtG), and phosphatidylethanol (PEth) in alternative biological matrices, focusing on the extraction and detection methods and full analytical conditions used.

Read Full Article
Back to Table of Contents

11. Computer-Delivered Screening and Brief Intervention for Alcohol Use in Pregnancy: A Pilot Randomized Trial.

ABSTRACT

BACKGROUND:
Although screening and brief intervention (SBI) for unhealthy alcohol use has demonstrated efficacy in some trials, its implementation has been limited. Technology-delivered approaches are a promising alternative, particularly during pregnancy when the importance of alcohol use is amplified. The present trial evaluated the feasibility and acceptability of an interactive, empathic, video-enhanced, and computer-delivered SBI (e-SBI) plus 3 tailored mailings, and estimated intervention effects.

METHODS:
We recruited 48 pregnant women who screened positive for alcohol risk at an urban prenatal care clinic. Participants were randomly assigned to the e-SBI plus mailings or to a control session on infant nutrition, and were re-evaluated during their postpartum hospitalization. The primary outcome was 90-day period prevalence abstinence as measured by timeline follow-back interview.

RESULTS:
Participants rated the intervention as easy to use and helpful (4.7 to 5.0 on a 5-point scale). Blinded follow-up evaluation at childbirth revealed medium-size intervention effects on 90-day period prevalence abstinence (OR = 3.4); similarly, intervention effects on a combined healthy pregnancy outcome variable (live birth, normal birthweight, and no neonatal intensive care unit stay) were also of moderate magnitude in favor of e-SBI participants (OR = 3.3). As expected in this intentionally underpowered pilot trial, these effects were nonsignificant (p = 0.19 and 0.09, respectively).

CONCLUSIONS:
This pilot trial demonstrated the acceptability and preliminary efficacy of e-SBI plus tailored mailings for alcohol use in pregnancy. These findings mirror the promising results of other trials using a similar approach and should be confirmed in a fully powered trial.

Read Full Article
Back to Table of Contents
12. **Reduction of Nfia gene expression and subsequent target genes by binge alcohol in the fetal brain**

Mandal C, Park JH, Lee HT, Seo H, Chung IY, Choi IG, Jung KH, Chai YG. (Republic of Korea); address: ygchai@hanyang.ac.kr

**ABSTRACT**

The objective of the present study was to investigate the changes in gene expression in the fetal brain (forebrain and hippocampus) caused by maternal binge alcohol consumption. Pregnant C57BL/6J mice were treated intragastrically with distilled phosphate-buffered saline (PBS) or ethanol (2.9 g/kg) from embryonic day (ED) 8-12. Microarray analysis revealed that a significant number of genes were altered at ED 18 in the developing brain. Specifically, in hippocampus, nuclear factor one alpha (Nfia) and three N-methyl-D-aspartate (Nmda) receptors (Nmdar1, Nmdar2b, and Nmdar2d) were down-regulated. The transcription factor Nfia controls gliogenesis, cell proliferation and Nmda-induced neuronal survival by regulating the expression of target genes. Some of the Nfia-target gene (Aldh1a, Folh1, Gjb6, Fgf1, Neurod1, Sept4, and Ntsr2) expressions were also altered as expected. These results suggest that the altered expression of Nfia and Nmda receptors may be associated with the etiology of fetal alcohol syndrome (FAS). The data presented in this report will contribute to the understanding of the molecular mechanisms associated with the effects of alcohol in FASD individuals.

Read Full Article


13. **Proceedings of the 2014 Annual Meeting of the Fetal Alcohol Spectrum Disorders Study Group**

Reynolds JN, Valenzuela CF, Medina AE, Wozniak JR. (USA); address: jnr@queensu.ca

**ABSTRACT**

The 2014 Fetal Alcohol Spectrum Disorders Study Group (FASDSG) meeting focused on the dual themes of the risks associated with low to moderate alcohol exposure during pregnancy and knowledge translation practices to enhance the impact of scientific research. The meeting theme was titled "Low drinking versus no drinking: Matching science with policy and public perception." Despite decades of basic science and clinical evidence that has documented the risks associated with prenatal alcohol exposure, there still exists confusion and uncertainty on the part of health professionals and the public regarding the question of whether or not there is a "safe" level of alcohol consumption during pregnancy. The first keynote presentation reviewed the data obtained from large-scale epidemiological studies that have attempted to address the question of relative risk associated with low to moderate alcohol exposure during pregnancy. This presentation was followed by an expert panel discussion of the state of scientific evidence obtained from clinical and basic science investigations concerning this question, and strategies for moving research evidence into policy and practice. The second keynote presentation presented a framework for knowledge translation and mobilization to move research discoveries toward implementation. The conference also featured updates by government agencies, FASt data talks that highlighted new and innovative findings in FASD research, and award presentations, including a lifetime achievement award presented to Dr. Kenneth Warren to acknowledge his longstanding support for FASD research. A highlight of the meeting was the presentation of the 2014 Henry Rosett award to Dr. Philip May in recognition of his substantial contributions to epidemiological studies on FASD.

Read Full Article
14. **Placental Fatty Acid ethyl esters are elevated with maternal alcohol use in pregnancies complicated by prematurity**

Gauthier TW, Mohan SS, Gross TS, Harris FL, Guidot DM, Brown LA (USA)

**ABSTRACT**

The accumulation of fatty acid ethyl esters (FAEEs) in meconium of term newborns has been described as one potential biomarker of maternal alcohol use during pregnancy. FAEEs accumulate in multiple alcohol-exposed fetal tissues and in the placenta. Limited research has focused on the identification of the premature newborn exposed to alcohol in utero. We hypothesized that maternal alcohol use occurs in a significant proportion of premature deliveries and that this exposure can be detected as elevated placental FAEEs. The goals of this study were to 1) determine the prevalence of maternal alcohol use in the premature newborn and 2) investigate whether placental FAEEs could identify those newborns with fetal alcohol exposure. This prospective observational study evaluated 80 placentas from 80 women after premature delivery. Subjects were interviewed for alcohol intake and placental FAEEs were quantified via GC/MS. Receiver Operator Characteristic (ROC) Curves were generated to evaluate the ability of placental FAEEs to predict maternal drinking during pregnancy. Adjusted ROC curves were generated to adjust for gestational age, maternal smoking, and illicit drug use. 30% of the subjects admitted to drinking alcohol during pregnancy and approximately 14% answered questions indicative of problem drinking (designated AUDIT+). The specific FAEEs ethyl stearate and linoleate, as well as combinations of oleate + linoleate + linolenate (OLL) and of OLL + stearate, were significantly (p<0.05) elevated in placentas from AUDIT+ pregnancies. Adjusted ROC Curves generated areas under the curve ranging from 88-93% with negative predictive values of 97% for AUDIT+ pregnancies. We conclude that nearly one third of premature pregnancies were alcohol-exposed, and that elevated placental FAEEs hold great promise to accurately determine maternal alcohol use, particularly heavy use, in pregnancies complicated by premature delivery.

Read Full Article

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4433254/

15. **Effects of Ethanol on the Cerebellum: Advances and Prospects**

Luo J; jialuo888@uky.edu (USA)

**ABSTRACT**

Alcohol abuse causes cerebellar dysfunction and cerebellar ataxia is a common feature in alcoholics. Alcohol exposure during development also impacts the cerebellum. Children with fetal alcohol spectrum disorder (FASD) show many symptoms associated specifically with cerebellar deficits. However, the cellular and molecular mechanisms are unclear. This special issue discusses the most recent advances in the study of mechanisms underlying alcohol-induced cerebellar deficits. The alteration in GABAA receptor-dependent neurotransmission is a potential mechanism for ethanol-induced cerebellar dysfunction. Recent advances indicate ethanol-induced increases in GABA release are not only in Purkinje cells (PCs), but also in molecular layer interneurons and granule cells. Ethanol is shown to disrupt the molecular events at the mossy fiber - granule cell - Golgi cell (MGG) synaptic site and granule cell parallel fibers - PCs (GPP) synaptic
site, which may be responsible for ethanol-induced cerebellar ataxia. Aging and ethanol may affect the smooth endoplasmic reticulum (SER) of PC dendrites and cause dendritic regression. Ethanol withdrawal causes mitochondrial damage and aberrant gene modifications in the cerebellum. The interaction between these events may result in neuronal degeneration, thereby contributing to motoric deficit. Ethanol activates doublestranded RNA (dsRNA)-activated protein kinase (PKR) and PKR activation is involved ethanol-induced neuroinflammation and neurotoxicity in the developing cerebellum. Ethanol alters the development of cerebellar circuitry following the loss of PCs, which could result in modifications of the structure and function of other brain regions that receive cerebellar inputs. Lastly, choline, an essential nutrient is evaluated for its potential protection against ethanol-induced cerebellar damages. Choline is shown to ameliorate ethanol-induced cerebellar dysfunction when given before ethanol exposure.

Read Full Article

Back to Table of Contents


16. Editorial: Genetics and epigenetics of fetal alcohol spectrum disorders
Mason S, Zhou FC (USA)

ABSTRACT
Children born to mothers who drink during pregnancy are at risk for growth retardation, memory, learning, and cognitive deficits under a lifelong disability known as Fetal Alcohol Spectrum Disorders (FASD), which occurs at a high rate in the US (~1/100 live births) and worldwide. There are three outstanding features of FASD. (a) Humans have been associated with alcohol consumption dated as far back as 7000 BC (McGovern et al., 2004) and there is no sign of waning. (b) FASD can range across a large spectrum of severity, from the more severe Fetal Alcohol Syndrome (FAS) (encompassing facial, brain, and gross deformity) to the hard to detect, subtle mental dysfunctions. The Centers for Disease Control and Prevention (CDC) indicates that approximately 7–8% of pregnant women consume alcohol in US, but diagnosed FASD occurs in a much smaller percentage (CDC, 2012). There is strong evidence to indicate that genetic makeup is a major contributing factor to the differential vulnerability to FASD. (c) Alcohol's deleterious effect has recently been found to go beyond cellular toxicity, to affect epigenetics. The epigenetic chemical code, methylation and acetylation written on top of genomic base elements (e.g., DNA cytosine and histone tails), can confer 3D DNA packaging and fundamentally alter gene transcription. Alcohol has recently been recognized to have strong influences on methylation and acetylation (see Resendiz et al., 2014a) via alcohol metabolism. Furthermore, current evidence points to alcohol's influence on the interaction of genetic and epigenetic factors. These fascinating new views are the center of this eBook, which includes new data and an in-depth discussion of the recent findings and expert opinions. It is hoped that by elucidating the genetic x epigenetic (GxE) interaction at the center of fetal alcohol exposure, new insight will lead the community of scientists toward a greater understanding of this disease, and lay a foundation for prospective new treatments and interventions.

Read Full Article
http://journal.frontiersin.org/article/10.3389/fgene.2015.00146/full

Back to Table of Contents


17. Hippocampal neuron populations are reduced in vervet monkeys with fetal alcohol exposure.
Burke MW, Ptito M, Ervin FR, Palmour RM. (USA)
ABSTRACT
Prenatal exposure to beverage alcohol is a major cause of mild mental retardation and developmental delay. In nonendangered alcohol-preferring vervet monkeys, we modeled the most common nondysmorphic form of fetal alcohol syndrome disorder with voluntary drinking during the third trimester of pregnancy. Here, we report significant numerical reductions in the principal hippocampal neurons of fetal alcohol-exposed (FAE) offspring, as compared to age-matched, similarly housed conspecifics with isocaloric sucrose exposure. These deficits, particularly marked in CA1 and CA3, are present neonatally and persist through infancy (5 months) and juvenile (2 years) stages. Although the volumes of hippocampal subdivisions in FAE animals are not atypical at birth, by age 2, they are only 65-70% of those estimated in age-matched controls. These data suggest that moderate, naturalistic alcohol consumption during late pregnancy results in a stable loss of hippocampal neurons and a progressive reduction of hippocampal volume.

Read Full Article

Back to Table of Contents


18. Sonographic findings in an isolated widened fetal subarachnoid space
Tongsong T, Puntachai P, Tongprasert F, Srisupundit K, Luewan S, Traisirisilp K. (Thailand)
theera.t@cmu.ac.th

ABSTRACT
The purpose of this series was to describe sonographic features of an isolated widened fetal subarachnoid space with a thin cerebral mantle and possible associations. Between January 2004 and December 2013, fetuses with a prenatal diagnosis of a widened subarachnoid space were prospectively recruited and followed. Histories of medical and familial diseases, as well as other demographic data such as drug exposure and lifestyles, were assessed and prospectively recorded. The women were investigated for possible associated factors. Ten pregnant women were recruited. Their fetuses showed various degrees of a widened subarachnoid space, ranging from 5 to 20 mm. Nearly all were diagnosed in the second half of pregnancy. Four cases had normal brain structures documented at midpregnancy anomaly screening. Only 1 case had a prenatal diagnosis of a widened subarachnoid space at 20 weeks' gestation. Two fetuses had exposure to alcohol in utero; 2 were proven to have cytomegalovirus infection; 1 had subarachnoid hemorrhage secondary to maternal use of warfarin; and 1 had a diagnosis of lissencephaly. Only 1 case in this series had normal postnatal development. A prenatal series of fetal widened subarachnoid spaces with possible associated factors is described. Although such relationships were not fully proven, they should be index cases for future studies.

Read Full Article

Back to Table of Contents

J Epidemiol Community Health doi:10.1136/jech-2014-203938

19. Alcohol consumption during pregnancy and adverse neurodevelopmental outcomes
Vall O, Salat-Battle J, Garcia-Algar O  (Spain); 90458@hospitaldelmar.cat

www.nofas-uk.org
ABSTRACT
Lack of evidence is not the same as evidence of absence of risk and, in this case, no evidence of harm does not mean evidence of no harm; subsequently, no amount of alcohol during pregnancy can be considered safe based on research evidence. Newborns exposed to maternal alcohol during pregnancy can develop a spectrum of characteristic facial features, impaired neurodevelopment, cognitive and behavioural disabilities, and fetal growth restriction known as fetal alcohol spectrum disorder (FASD), with the most severe form, including specific morphological facial abnormalities, defined as fetal alcohol syndrome (FAS). However, most patients with FASD exhibit only a subset of the characteristics of FAS, such as cognitive and behavioural deficits, and, possibly, facial abnormalities. FASD and FAS represent the most recurrent and easily preventable cause of acquired development disabilities in newborns. It is a serious problem for the individual and for society; it entails not only human suffering but also loss of productivity, and a high burden of medical and social costs. There are several unsolved questions related to prenatal alcohol exposure and adverse neurodevelopmental outcomes. The true rate of prenatal alcohol consumption in different countries using reliable tools of estimation is unknown. It is recognised that FASD is entirely preventable through alcohol abstinence, but worldwide 30% (60% in certain countries) of pregnant women consume alcohol during pregnancy. In Canada, prevalence rates of FAS and FASD have been reported to be 1–3 and 9 per 1000 live births, respectively, higher than the FAS prevalence of 0.5–2.0 per 1000 live infants in the USA. Currently, in Europe, there are no systematic data on FAS and FASD prevalence rates, nor on prenatal exposure to ethanol, and only one retrospective study in Italy showed a prevalence of FAS.

Read Full Article http://jech.bmj.com/content/early/2015/04/22/jech-2014-203938.extract

Back to Table of Contents


20. Developmental exposure to ethanol increases the neuronal vulnerability to oxygen-glucose deprivation in cerebellar granule cell cultures

Le Duc D, Spataru A, Ceanga M, Zagrean L, Schöneberg T, Toescu EC, Zagrean AM (Germany, Romania, UK); diana_leduc@eva.mpg.de, azagrean@umf.ro

ABSTRACT
Prenatal alcohol exposure is associated with microencephaly, cognitive and behavioral deficits, and growth retardation. Some of the mechanisms of ethanol-induced injury, such as high level oxidative stress and overexpression of pro-apoptotic genes, can increase the sensitivity of fetal neurons towards hypoxic/ischemic stress associated with normal labor. Thus, alcohol-induced sequelae may be the cumulative result of direct ethanol toxicity and increased neuronal vulnerability towards metabolic stressors, including hypoxia. We examined the effects of ethanol exposure on the fetal cerebellar granular neurons’ susceptibility to hypoxic/hypoglycemic damage. A chronic ethanol exposure covered the entire prenatal period and 5 days postpartum through breastfeeding, a time interval partially extending into the third-trimester equivalent in humans. After a binge-like alcohol exposure at postnatal day 5, glutamatergic cerebellar granule neurons were cultured and grown for 7 days in vitro, then exposed to a 3-h oxygen-glucose deprivation to mimic a hypoxic/ischemic condition. Cellular viability was monitored by dynamic recording of propidium iodide fluorescence over 20h reoxygenation. We explored differentially expressed genes on microarray data from a mouse embryonic ethanol-exposure model and validated these by real-time PCR on the present model. In the ethanol-treated cerebellar granule neurons we find an increased expression of genes related to apoptosis (Mapk8 and Bax), but also of genes previously described as neuroprotective (Dhcr24 and Bdnf), which might suggest an actively maintained viability. Our
data suggest that neurons exposed to ethanol during development are more vulnerable to in vitro hypoxia/hypoglycemia and have higher intrinsic death susceptibility than unexposed neurons.

Read Full Article

Back to Table of Contents


21. Fetal programming and cardiovascular pathology
Alexander BT, Dasinger JH, Intapad S. (USA)

ABSTRACT
Low birth weight serves as a crude proxy for impaired growth during fetal life and indicates a failure for the fetus to achieve its full growth potential. Low birth weight can occur in response to numerous etiologies that include complications during pregnancy, poor prenatal care, parental smoking, maternal alcohol consumption, or stress. Numerous epidemiological and experimental studies demonstrate that birth weight is inversely associated with blood pressure and coronary heart disease. Sex and age impact the developmental programming of hypertension. In addition, impaired growth during fetal life also programs enhanced vulnerability to a secondary insult. Macrosomia, which occurs in response to maternal obesity, diabetes, and excessive weight gain during gestation, is also associated with increased cardiovascular risk. Yet, the exact mechanisms that permanently change the structure, physiology, and endocrine health of an individual across their lifespan following altered growth during fetal life are not entirely clear. Transmission of increased risk from one generation to the next in the absence of an additional prenatal insult indicates an important role for epigenetic processes. Experimental studies also indicate that the sympathetic nervous system, the renin angiotensin system, increased production of oxidative stress, and increased endothelin play an important role in the developmental programming of blood pressure in later life. Thus, this review will highlight how adverse influences during fetal life and early development program an increased risk for cardiovascular disease including high blood pressure and provide an overview of the underlying mechanisms that contribute to the fetal origins of cardiovascular pathology.

Read Full Article

Back to Table of Contents


22. Sustained action of developmental ethanol exposure on the cortisol response to stress in zebrafish larvae and adults.
Baiamonte M, Brennan CH, Vinson GP. (UK)

ABSTRACT
BACKGROUND:
Ethanol exposure during pregnancy is one of the leading causes of preventable birth defects, leading to a range of symptoms collectively known as fetal alcohol spectrum disorder. More moderate levels of prenatal ethanol exposure lead to a range of behavioural deficits including aggression, poor social interaction, poor cognitive performance and increased likelihood of addiction in later life. Current theories suggest that adaptation in the hypothalamo-pituitary-adrenal (HPA) axis and neuroendocrine systems contributes to mood alterations underlying behavioural deficits and
vulnerability to addiction. In using zebrafish (Danio rerio), the aim is to determine whether developmental ethanol exposure provokes changes in the hypothalamo-pituitary-interrenal (HPI) axis (the teleost equivalent of the HPA), as it does in mammalian models, therefore opening the possibilities of using zebrafish to elucidate the mechanisms involved, and to test novel therapeutics to alleviate deleterious symptoms.

RESULTS AND CONCLUSIONS:

The results showed that developmental exposure to ambient ethanol, 20mM-50mM 1-9 days post fertilisation, had immediate effects on the HPI, markedly reducing the cortisol response to air exposure stress, as measured by whole body cortisol content. This effect was sustained in adults 6 months later. Morphology, growth and locomotor activity of the animals were unaffected, suggesting a specific action of ethanol on the HPI. In this respect the data are consistent with mammalian results, although they contrast with the higher corticosteroid stress response reported in rats after developmental ethanol exposure. The mechanisms that underlie the specific sensitivity of the HPI to ethanol require elucidation.

Read Full Article
Back to Table of Contents


23. Frequency and epidemiologic aspects of male infertility.

Sohrabvand F, Jafari M, Shariat M, Haghiollahi F, Lotfi M (Iran); valrec2@yahoo.com

ABSTRACT

According to different geographical conditions, human health in different sub-regions of the world and cultural differences, the male factor infertility has heterogeneous causes in the world. This study was performed in an attempt to clarify the associated factors which might play a role in this respect in a group of Iranian infertile men. This study was a cross-sectional, descriptive and retrospective study. The information was obtained from the men who had attended the clinic from March 2004-2006. The factors which were studied in this research are the demographic characteristics, smoking, addiction, alcohol drinking, and exposure to lead, cimetidine and history of surgery. In 23.7 % of couples the cause of infertility was pure male factor and in 19.3 % of them the problem was related to male and female factor both. The most important associated factors for male factor included smoking (29%) and history of varicocele operation (22%). Since the quality of individual and social life is related to fertility state, it seems that more comprehensive studies on factors affecting male fertility at the community level are justified and recommended.

Read Full Article
Back to Table of Contents


24. Postnatal ethanol exposure alters levels of 2-arachidonylglycerol-metabolizing enzymes and pharmacological inhibition of monoacylglycerol lipase does not cause neurodegeneration in neonatal mice

Subbanna S, Psychoyos D, Xie S, Basavarajappa BS. (USA)

ABSTRACT

The consumption of ethanol by pregnant women may cause neurological abnormalities, affecting learning and memory processes in children, and are collectively described as fetal alcohol spectrum disorders (FASD). However, ethanol administration to neonatal animals is not equivalent to exposure during pregnancy, as the alcohol can pass through the placenta and enter the bloodstream during the fetal period. In this study, we investigated the effect of postnatal ethanol exposure on the activity of 2-arachidonylglycerol-metabolizing enzymes and on the expression of monoacylglycerol lipase (MGL) in the neonatal mice. Results showed that ethanol exposure on the neonatal mice increased the expression of MGL and reduced the activity of 2-arachidonylglycerol-metabolizing enzymes. However, pharmacological inhibition of MGL did not cause neurodegeneration in neonatal mice.
disorders. However, the molecular mechanisms underlying these changes are still poorly understood. In our previous studies, we found that ethanol treatment of postnatal day 7 (P7) mice significantly enhances the anandamide levels but not the 2-arachidonylglycerol (2-AG) levels and induces widespread neurodegeneration, but the reason for the lack of significant effects of ethanol on the 2-AG level is unknown. In this study, we examined developmental changes in diacylglycerol lipase-α, β (DAGL-α and β) and monoacylglycerol lipase (MAGL). We found that the levels of these proteins were significantly higher in adult brains compared to those detected early in brain development. Next, we examined the influence of P7 ethanol treatment on these enzymes, finding that it differentially altered the DAGL-α protein and mRNA levels but consistently enhanced those of the DAGL-β. Interestingly, the ethanol treatment enhanced MAGL protein and mRNA levels. Inhibition of MAGL with KML29 failed to induce neurodegeneration in P7 mice. Collectively, these findings suggest that ethanol significantly activates DAGL-β and MAGL in the neonatal brain, resulting in no net change in 2-AG levels. The consumption of ethanol by pregnant women may cause neurological abnormalities, affecting learning and memory processes in children, and are collectively described as fetal alcohol spectrum disorders (FASDs). In our study, ethanol treatment of postnatal day 7 (P7) mice significantly enhanced the levels of the developmentally relevant endocannabinoids anandamide (AEA) but not 2-arachidonylglycerol (2-AG), and induced widespread neurodegeneration, yet the reason for the lack of effects of ethanol on the 2-AG level is unknown. Here, the ethanol treatment of P7 mice causes the specific up-regulation of AEA-CB1R signaling over the 2-AG-CB1R pathway by the specific reorganization of the enzymes that synthesize (DAGL-α/β) and degrade (MAGL) 2-AG. This study demonstrates the neuro-regulatory role of 2-AG metabolizing enzymes in ethanol-induced neurodegeneration in neonatal mice.

Read Full Article

Back to Table of Contents


25. Transient activation of microglia following acute alcohol exposure in developing mouse neocortex is primarily driven by BAX-dependent neurodegeneration.
Ahlers KE, Karaçay B, Fuller L, Bonthius DJ, Dailey ME. (USA)

ABSTRACT
Fetal alcohol exposure is the most common known cause of preventable mental retardation, yet we know little about how microglia respond to, or are affected by, alcohol in the developing brain in vivo. Using an acute (single day) model of moderate (3 g/kg) to severe (5 g/kg) alcohol exposure in postnatal day (P) 7 or P8 mice, we found that alcohol-induced neuroapoptosis in the neocortex is closely correlated in space and time with the appearance of activated microglia near dead cells. The timing and molecular pattern of microglial activation varied with the level of cell death. Although microglia rapidly mobilized to contact and engulf late-stage apoptotic neurons, apoptotic bodies temporarily accumulated in neocortex, suggesting that in severe cases of alcohol toxicity the neurodegeneration rate exceeds the clearance capacity of endogenous microglia. Nevertheless, most dead cells were cleared and microglia began to deactivate within 1-2 days of the initial insult. Coincident with microglial activation and deactivation, there was a transient increase in expression of pro-inflammatory factors, TNFα and IL-1β, after severe (5 g/kg) but not moderate (3 g/kg) EtOH levels. Alcohol-induced microglial activation and pro-inflammatory factor expression were largely abolished in BAX null mice lacking neuroapoptosis, indicating that microglial activation is primarily triggered by apoptosis rather than the alcohol. Therefore, acute alcohol exposure in the developing neocortex causes transient microglial activation and mobilization, promoting clearance of dead cells and tissue recovery. Moreover, cortical microglia show a remarkable capacity to rapidly deactivate following even severe neurodegenerative insults in the developing brain. GLIA 2015.

Read Full Article

Back to Table of Contents

www.nofas-uk.org
26. Fetal alcohol spectrum disorders in Australia - the future is prevention.
Elliott EJ.; elizabeth.elliott@health.nsw.gov.au (Australia)

ABSTRACT
Fetal alcohol spectrum disorders (FASD) are increasingly recognised throughout Australia as important, but preventable, disorders that result in lifelong problems with health and learning, mental health, behaviour and substance misuse. The role of this article is to highlight current efforts, which are in their infancy, to recognise and prevent FASD in Australia. A federal parliamentary inquiry into FASD (2011), development of an Australian Government ‘action plan’ to prevent FASD (2013) and the announcement in June 2014 of government funding to progress the plan and appoint a National FASD Technical Network have focused attention on the need for FASD prevention in Australia. Other welcome developments include the formation of Parliamentarians for the Prevention of FASD (2011), revision of guidelines regarding alcohol use in pregnancy by the National Health and Medical Research Council (NHMRC; 2009) and provision of targeted funding for FASD research by the NHMRC (2013). Initiatives by Indigenous communities to restrict access to alcohol and diagnose and prevent FASD have had a significant impact in high-risk communities. The National Organisation for FASD has an important ongoing advocacy and educational remit. Nongovernment organisations such as the Foundation for Alcohol Research and Education have contributed to prevention by developing resources to assist health professionals to advise women about the harms of alcohol use in pregnancy; encouraging men to abstain from alcohol during the pregnancy; drafting a national plan; and advocating for pregnancy warning labels on alcohol. Internationally, in 2014, a charter on prevention of FASD was published in The Lancet Global Health, and the World Health Organization released guidelines for identification and management of substance use in pregnancy.

Early recognition and support for individuals with FASD is crucial to prevent adverse secondary outcomes; however, primary prevention of alcohol use in pregnancy, and hence FASD, should be our future goal. The causal pathway to drinking in pregnancy is complex and requires a broad social ecological approach. Prevention will take time, must involve all government sectors and should incorporate primary, secondary and tertiary strategies to target both the broader community and populations at high risk of alcohol use during pregnancy.

Read Full Article

Back to Table of Contents
cost for corrections was then applied to the estimated number of youths and adults with FASD in custody. The cost of corrections among youths with FASD in Canada in 2011/2012 was calculated to be approximately $17.5M Canadian dollars (CND; $13.6M CND for males and $3.8M CND for females) and among adults with FASD was estimated to be about $356.2M CND ($140M CND for provincial and territorial custody and $216.2M CND for federal custody). The study findings emphasize the need to raise awareness regarding the prevalence of FASD in the correctional system. It is crucial to incorporate FASD screening and intervention strategies as early as possible in the criminal justice process.

Read Full Article

Back to Table of Contents

---


du Plessis L, Jacobson SW, Molteno CD, Robertson FC, Peterson BS, Jacobson JL, Meintjes EM. (South Africa, USA)

ABSTRACT

OBJECTIVES:

Classical eyeblink conditioning (EBC), an elemental form of learning, is among the most sensitive indicators of fetal alcohol spectrum disorders. The cerebellum plays a key role in maintaining timed movements with millisecond accuracy required for EBC. Functional MRI (fMRI) was used to identify cerebellar regions that mediate timing in healthy controls and the degree to which these areas are also recruited in children with prenatal alcohol exposure.

EXPERIMENTAL DESIGN:

fMRI data were acquired during an auditory rhythmic/non-rhythmic finger tapping task. We present results for 17 children with fetal alcohol syndrome (FAS) or partial FAS, 17 heavily exposed (HE) nonsyndromal children and 16 non- or minimally exposed controls.

PRINCIPAL OBSERVATIONS:

Controls showed greater cerebellar blood oxygen level dependent (BOLD) activation in right crus I, vermis IV-VI, and right lobule VI during rhythmic than non-rhythmic finger tapping. The alcohol-exposed children showed smaller activation increases during rhythmic tapping in right crus I than the control children and the most severely affected children with either FAS or PFAS showed smaller increases in vermis IV-V. Higher levels of maternal alcohol intake per occasion during pregnancy were associated with reduced activation increases during rhythmic tapping in all four regions associated with rhythmic tapping in controls.

CONCLUSIONS:

The four cerebellar areas activated by the controls more during rhythmic than non-rhythmic tapping have been implicated in the production of timed responses in several previous studies. These data provide evidence linking binge-like drinking during pregnancy to poorer function in cerebellar regions involved in timing and somatosensory processing needed for complex tasks requiring precise timing.

Read Full Article

Back to Table of Contents

www.nofas-uk.org

ABSTRACT

BACKGROUND:
Fatty acids (FAs) are essential for fetal growth. Exposure to perfluorinated chemicals (PFCs) may disrupt FA homeostasis, but there is no epidemiological data regarding associations of PFCs and FA concentrations.

OBJECTIVES:
We estimated associations between perfluorooctane sulfonate (PFOS)/perfluorooctanoate (PFOA) concentrations and maternal levels of FAs and triglyceride (TG) and birth size of the offspring.

METHODS:
306 mother-child pairs were analyzed in this birth cohort between 2002 and 2005 in Japan. The prenatal PFOS and PFOA levels were measured in maternal serum samples by liquid chromatography-tandem mass spectrometry. Maternal blood levels of 9 FAs and TG were measured by gas chromatography-mass spectrometry and TG-IE kits, respectively. Information of infants' birth size were obtained from participant medical records.

RESULTS:
The median PFOS and PFOA levels were 5.6 and 1.4 ng/mL, respectively. In the fully adjusted model, including maternal age, parity, annual household income, blood sampling period, alcohol consumption and smoking during pregnancy, PFOS, not PFOA, had a negative association with the levels of palmitic, palmitoleic, oleic, linoleic, α-linolenic, and arachidonic acids (p <0.005) and TG (p value=0.016). Females weighed 186.6 g less in mothers whose PFOS levels were in the fourth quartile compared to the first quartile (95% CI: -363.4, -9.8). We observed no significant association between maternal levels of PFOS and birth weight of male infants.

CONCLUSIONS:
Our data suggest an inverse association between PFOS exposure and polyunsaturated FA levels in pregnant women. We also found a negative association between maternal PFOS levels and female birth weight.

Read Full Article

Back to Table of Contents

30. The effects of postnatal alcohol exposure and galantamine on the context pre-exposure facilitation effect and acetylcholine efflux using in vivo microdialysis.
Perkins AE, Fadel JR, Kelly SJ.; address: sandra-kelly@sc.edu (USA)

ABSTRACT
Fetal alcohol spectrum disorders (FASD) are characterized by damage to multiple brain regions, including the hippocampus, which is involved in learning and memory. The acetylcholine neurotransmitter system provides major input to the hippocampus and is a possible target of developmentalalcohol exposure. Alcohol (3.0 g/kg/day) was administered via intubation to male rat
pups (postnatal day [PD] 2-10; ethanol-treated [ET]). Controls received a sham intubation (IC) or no treatment (NC). Acetylcholine efflux was measured using in vivo microdialysis (PD 32-35). ET animals were not different at baseline, but had decreased K(+)Ca(2+)-induced acetylcholine efflux compared to NC animals and an enhanced acetylcholine response to galantamine (acetylcholinesterase inhibitor; 2.0 mg/kg) compared to both control groups. A separate cohort of animals was tested in the context pre-exposure facilitation effect task (CPFE; PD 30-32) following postnatal alcohol exposure and administration of galantamine (2.0 mg/kg; PD 11-30). Neither chronic galantamine nor postnatal alcohol exposure influenced performance in the CPFE task. Using immunohistochemistry, we found that neither alcohol exposure nor behavioral testing significantly altered the density of vesicular acetylcholine transporter or alpha7 nicotinic acetylcholine receptor in the ventral hippocampus (CA1). In the medial septum, the average number of choline acetyltransferase (ChAT+) cells was increased in ET animals that displayed the context-shock association; there were no changes in IC and NC animals that learned the context-shock association or in any animals that were in the control task that entailed no learning. Taken together, these results indicate that the hippocampal acetylcholine system is significantly disrupted under conditions of pharmacological manipulations (e.g., galantamine) in alcohol-exposed animals. Furthermore, ChAT was up-regulated in ET animals that learned the CPFE, which may account for their ability to perform this task. In sum, developmental alcohol exposure may disrupt learning and memory in adolescence via a cholinergic mechanism.

Read Full Article

Lewis CE1, Thomas KG, Dodge NC, Molteno CD, Meintjes EM, Jacobson JL, Jacobson SW. (South Africa)

ABSTRACT

BACKGROUND:
Previous studies using the California Verbal Learning Test-Children's Version (CVLT-C) to examine effects of heavy prenatal alcohol exposure on verbal learning and memory have reported impaired information acquisition (i.e., encoding), rather than retrieval, as the primary mechanism underlying learning and memory impairment. We administered the CVLT-C to 2 independent cohorts to determine whether (i) effects on encoding are also seen at moderate exposure levels, using both categorical (diagnostic/exposure group) and continuous exposure measures; (ii) these deficits are specific or secondary to alcohol-related impairment in IQ; (iii) effects on retrieval can be detected over and above effects on initial encoding; and (iv) effects on learning are attributable to less efficient learning strategy use.

METHODS:
We administered the CVLT-C and Wechsler Intelligence Scale for Children to 151 Cape Town heavy and nonexposed children (M = 10.3 years), and 291 Detroit adolescents recruited to over-represent moderate-to-heavy prenatal alcohol exposure (M = 14.4 years).

RESULTS:
Effects on encoding in the heavily exposed Cape Town cohort and on retrieval in both cohorts were significant after adjustment for IQ. Although effects on retrieval were no longer significant in Cape Town after control for initial encoding, effects on recognition memory continued to be evident in Detroit. Children with full or partial fetal alcohol syndrome were less able to use the semantic cluster encoding strategy implicit in the CVLT-C.

CONCLUSIONS:
Effects on verbal learning were seen primarily in the more heavily exposed Cape Town cohort; effects on recall and recognition memory were also seen at moderate exposure levels in Detroit. These effects were not attributable to alcohol-related impairment in overall intellectual competence. The finding that effects on retention continued to be evident after statistical adjustment for initial encoding in Detroit suggests that a fetal alcohol-related deficit in retrieval is not secondary to a failure to encode the initial information. These data confirm that this impairment in initial learning is mediated, in part, by failure to use the semantic cluster learning strategy.

Read Full Article

32. Eye movements reveal sexually dimorphic deficits in children with fetal alcohol spectrum disorder.
Paolozza A, Munn R, Munoz DP, Reynolds JN. (Canada)

ABSTRACT
BACKGROUND:
We examined the accuracy and characteristics of saccadic eye movements in children with fetal alcohol spectrum disorder (FASD) compared with typically developing control children. Previous studies have found that children with FASD produce saccades that are quantifiably different from controls. Additionally, animal studies have found sex-based differences for behavioral effects after prenatal alcohol exposure. Therefore, we hypothesized that eye movement measures will show sexually dimorphic results.

METHODS:
Children (aged 5-18 years) with FASD (n = 71) and typically developing controls (n = 113) performed a visually-guided saccade task. Saccade metrics and behavior were analyzed for sex and group differences.

RESULTS:
Female control participants had greater amplitude saccades than control males or females with FASD. Accuracy was significantly poorer in the FASD group, especially in males, which introduced significantly greater variability in the data. Therefore, we conducted additional analyses including only those trials in which the first saccade successfully reached the target within a ± 1° window. In this restricted amplitude dataset, the females with FASD made saccades with significantly lower velocity and longer duration, whereas the males with FASD did not differ from the control group. Additionally, the mean and peak deceleration were selectively decreased in the females with FASD.

CONCLUSIONS:
These data support the hypothesis that children with FASD exhibit specific deficits in eye movement control and sensory-motor integration associated with cerebellar and/or brain stem circuits. Moreover, prenatal alcohol exposure may have a sexually dimorphic impact on eye movement metrics, with males and females exhibiting differential patterns of deficit.

Read Full Article
33. Reduced DNA methylation at the PEG3 DMR and KvDMR1 loci in children exposed to alcohol in utero: a South African Fetal Alcohol Syndrome cohort study.
Masemola ML, van der Merwe L, Lombard Z, Viljoen D, Ramsay M. (South Africa)

ABSTRACT
Fetal alcohol syndrome (FAS) is a devastating developmental disorder resulting from alcohol exposure during fetal development. It is a considerable public health problem worldwide and is characterized by central nervous system abnormalities, dysmorphic facial features, and growth retardation. Imprinted genes are known to play an important role in growth and development and therefore four imprinting control regions (ICRs), H19 ICR, IG-DMR, KvDMR1 and PEG3 DMR were examined. It is proposed that DNA methylation changes may contribute to developmental abnormalities seen in FAS and which persist into adulthood. The participants included FAS children and controls from the Western and Northern Cape Provinces. DNA samples extracted from blood and buccal cells were bisulfite modified, the ICRs were amplified by PCR and pyrosequencing was used to derive a quantitative estimate of methylation at selected CpG dinucleotides: H19 ICR (six CpG sites; 50 controls and 73 cases); KvDMR1 (7, 55, and 86); IG-DMR (10, 56, and 84); and PEG3 DMR (7, 50, and 79). The most profound effects of alcohol exposure are on neuronal development. In this study we report on epigenetic effects observed in blood which may not directly reflect tissue-specific alterations in the developing brain. After adjusting for age and sex (known confounders for DNA methylation), there was a significant difference at KvDMR1 and PEG3 DMR, but not the H19 ICR, with only a small effect (0.84% lower in cases; \(p = 0.035\)) at IG-DMR. The two maternally imprinted loci, KvDMR1 and PEG3 DMR, showed lower average locus-wide methylation in the FAS cases (1.49%; \(p < 0.001\) and 7.09%; \(p < 0.001\), respectively). The largest effect was at the PEG3 DMR though the functional impact is uncertain. This study supports the role of epigenetic modulation as a mechanism for the teratogenic effects of alcohol by altering the methylation profiles of imprinted loci in a locus-specific manner.

Read Full Article

Back to Table of Contents

34. The protective effect of vitamin E against prenatal and early postnatal ethanol treatment-induced heart abnormality in rats: A 3-month follow-up study.
Shirpoor A, Nemati S, Ansari MH, Ilkhanizadeh B. (Iran)

ABSTRACT
Ethanol consumption during pregnancy is associated with fetal heart malformation. However, the underlying mechanism of prenatal ethanol exposure causing heart malfunction is not well known. The current study examined the effect of prenatal and early postnatal ethanol consumption on heart abnormality resulting from oxidative and inflammatory stress. It was also intended to find out whether vitamin E inhibits the abnormality induced by ethanol in rats' heart tissue. Pregnant Wistar rats received ethanol with/without vitamin E from the seventh day of gestation (GD7) throughout lactation. The proliferation in heart muscle cells and coronary smooth muscle cells, protein carbonyl, IL-6, TNF-\(\alpha\), homocysteine levels, also lipid profile in heart and plasma of male pups were measured at the end of lactation (PN 21) and 90days after birth (PN 90). The results indicated proliferation of heart muscle and coronary smooth muscle cells along with heart structural alteration, protein oxidation, lipid peroxidation, inflammatory reaction, and hyperhomocysteinemia in offspring after 21 and 90days of birth compared with the controls. Vitamin E treatment significantly decreased cell proliferation and heart structural alteration, compared with the group treated by ethanol alone. Furthermore, it reduced the elevation of protein carbonyl, lipid peroxidation, and increased inflammatory proteins to levels as those of the controls. These findings strongly support the idea
that ethanol intake by dams during pregnancy and early postnatal days induces heart abnormality mediated by oxidative stress and inflammatory reactions, and that these effects can be alleviated by using vitamin E as an antioxidant and anti-inflammatory molecule.

Read Full Article
Back to Table of Contents


35. **Using a single binge drinking question to identify Russian women at risk for an alcohol-exposed pregnancy**.

Balachova T, Sobell LC, Agrawal S, Isurina G, Tsvetkova L, Volkova E, Bohora S; email: Tatiana-Balachova@ouhsc.edu; (Russia, USA)

**ABSTRACT**

**INTRODUCTION:**

Low rates of contraception and at-risk drinking place many Russian women at risk of an alcohol-exposed pregnancy (AEP). The only realistic way to determine when women are at risk of AEP is by self-reports. A U.S. study found that a single binge-drinking question (SBD) effectively identified nearly all women whose drinking placed them at risk of AEP.

**METHODS:**

The present study replicated the U.S.

**STUDY:**

Participants were 689 non-pregnant Russian women of childbearing age who were at AEP risk. Their answers to SBD, "During the previous three months, how often did you have four or more drinks on one occasion", were compared with their reports of binge drinking on a 90-day Timeline Followback (TLFB) calendar.

**RESULTS:**

The SBD identified 99% of at-risk Russian women as binge drinkers, replicating U.S.

**FINDINGS:**

Only 8% of the women were identified at-risk using a second AEP criterion of ≥8 drinks on average per week. Although Russian women did not report heavy weekly drinking and two-thirds did not meet AUDIT criteria for problem drinking, when they did drink, 40% of the time it was binge drinking.

**CONCLUSIONS:**

Almost all Russian women who were at risk of an AEP were identified by a single binge-drinking question. Results from this study suggest that Russian health care practitioners can use SBD to successfully screen women for AEP risk. SBD identified 99% of Russian women who were at AEP risk. Consequently, it is recommended that SBD be incorporated into routine health care screenings at OB/GYN clinic visits.

Read Full Article
Back to Table of Contents
36. Alcohol-induced histone H3K9 hyperacetylation and cardiac hypertrophy are reversed by a histone acetylases inhibitor anacardic acid in developing murine hearts.

Peng C, Zhang W, Zhao W, Zhu J, Huang X, Tian J.; address: jietyan@cqmu.edu.cn, (China)

ABSTRACT

BACKGROUND:
The expression of cardiac genes is precisely regulated, and any perturbation may cause development defects. In a previous study, we demonstrated that alcohol consumption during pregnancy could lead to uncontrolled expressions of cardiac genes and eventually result in cardiac dysplasia. However, the underlying mechanisms remain unclear. In the present study, we have investigated the alcohol-induced cardiac hypertrophy and its potential mechanisms. Furthermore, the protective effect of anacardic acid against the alcohol-induced cardiac hypertrophy has been explored in experimental mice.

METHODS AND RESULTS:
C57BL/6 pregnant mice were gavaged with 56% ethanol or saline and the hearts of their fetus were collected for analysis. Binding of p300, CBP, PCAF, SRC1, except GCN5, were increased to the NKX2.5 promoter in fetal mouse hearts exposed to alcohol. Increased acetylation of H3K9 and increased mRNA expression of NKX2.5, β-MHC and Cx43 were observed in the same samples. Treatment with a pan-acetylase inhibitor, anacardic acid, reduced the binding affinity of p300 and PCAF to the NKX2.5, β-MHC, Cx43 promoters and attenuated H3K9 hyperacetylation. Interestingly, anacardic acid down-regulated over-expression of these cardiac genes induced by alcohol and ultimately attenuated ethanol-induced cardiac hypertrophy in fetal mice.

CONCLUSIONS:
Our results indicate that alcohol exposure during pregnancy could lead to fetal cardiac hypertrophy. The over-expression of NKX2.5, β-MHC, Cx43 mediated by p300 and PCAF may be critical mechanisms of alcohol-induced cardiac hypertrophy. Anacardic acid can down-regulate the over-expression of cardiac genes and reverse cardiac hypertrophy caused by alcohol treatment in pregnant mice, suggesting it could be a potential therapeutic agent for the treatment of cardiac hypertrophy.

Read Full Article
Back to Table of Contents

37. Postnatal administration of allopregnanolone modifies glutamate release but not BDNF content in striatum samples of rats prenatally exposed to ethanol.

Yunes R, Estrella CR, García S, Lara HE, Cabrera R. (Argentina, Chile)

ABSTRACT

Ethanol consumption during pregnancy may induce profound changes in fetal CNS development. We postulate that some of the effects of ethanol on striatal glutamatergic transmission and neurotrophin expression could be modulated by allopregnanolone, a neurosteroid modulator of GABAA receptor activity. We describe the acute pharmacological effect of allopregnanolone (65 μg/kg, s.c.) administered to juvenile male rats (day 21 of age) on the corticostriatal glutamatergic pathway, in both control and prenatally ethanol-exposed rats (two ip injections of 2.9 g/kg in 24% v/v saline solution on gestational day 8). Prenatal ethanol administration decreased the K(+)‐induced release of glutamate regarding the control group. Interestingly, this effect was reverted by allopregnanolone. Regarding BDNF, allopregnanolone decreases the content of this neurotrophic

www.nofas-uk.org
factor in the striatum of control groups. However, both ethanol alone and ethanol plus allopregnanolone treated animals did not show any change regarding control values. We suggest that prenatal ethanol exposure may produce an alteration of GABAA receptors which blocks the GABA agonist-like effect of allopregnanolone on rapid glutamate release, thus disturbing normal neural transmission. Furthermore, the reciprocal interactions found between GABAergic neurosteroids and BDNF could underlie mechanisms operating during the neuronal plasticity of fetal development.

Read Full Article
Back to Table of Contents

38. Message on a bottle.
Burton A. (Australia)

ABSTRACT
Fetal alcohol spectrum disorder continues to cause problems—sometimes serious neurological problems—worldwide. But are mothers-to-be adequately informed about the dangers of drinking during pregnancy? Adrian Burton investigates.

Reduced fetal and postnatal growth, heart defects, facial deformity, and abnormal brain development that can lead to problems with cognition, movement, and social skills; these are among the outcomes of fetal alcohol spectrum disorder (FASD). In its worst form—fetal alcohol syndrome (FAS)—children may present with all these features. It’s entirely preventable if mothers-to-be don’t drink. But do prospective parents know that? Do they know that FASD exists at all?

Read Full Article
http://www.thelancet.com/journals/laneur/article/PIIS1474-4422(15)70055-4/fulltext
Back to Table of Contents

Soh DW, Skocic J, Nash K, Stevens S, Turner GR, Rovet J. (Canada)

ABSTRACT
Children with fetal alcohol spectrum disorder show executive function (EF) deficits, particularly in self-regulation skills, and abnormalities in brain regions critical for these skills. None of the validated EF interventions for these children has been evaluated with regards to impacts on brain structure. Twenty-nine children with FASD were assigned to either an immediate-treatment (TX) or delayed-treatment control (DTC) group (DTC). Nineteen typically developing children served as healthy controls (CT). All received a structural MRI scan and baseline neuropsychological testing, following which the TX group underwent 12 weekly 1.5-h sessions of the Alert Program for Self-Regulation®. After treatment or a period of ~14 weeks, all received a repeat scan and post-intervention testing. Whole-brain and region-of-interest analyses using voxel-based morphometry evaluated group differences and changes over time in gray matter (GM). Exploratory analyses revealed significant group changes: (1) At baseline, combined TX and DTC groups demonstrated global GM reductions compared with the CT group. (2) Region-of-interest analysis using a frontal mask, comparing post-intervention to pre-intervention results, showed significantly increased GM in the left middle frontal gyrus (BA10), right frontal pole (BA11), and right anterior cingulate (BA32) in the TX group. Similar results were not found in the DTC or CT groups. (3) At post-intervention, both TX and CT groups showed larger GM volumes than the DTC group in the left superior frontal gyrus (BA9), which was smaller in the FASD group at baseline. These results suggested that Alert led to
improvements in post-intervention testing of self-regulation skills and typical brain development in treated children

Read Full Article
Back to Table of Contents


Gidley Larson JC, Flaro L, Peterson RL, Connery AK, Baker DA, Kirkwood MW; michael.kirkwood@childrenscolorado.org; (USA)

ABSTRACT
Inadequate effort during neuropsychological examination results in inaccurate representations of an individual's true abilities and difficulties. As such, performance validity tests (PVTs) are strongly recommended as standard practice during adult-based evaluations. One concern with using PVTs with children is that failure reflects immature cognitive ability rather than non-credible effort. The current study examined performance on the Medical Symptom Validity Test (MSVT) in two large pediatric clinical samples with strikingly different neuropsychological profiles: (1) mild traumatic brain injury (mTBI; n = 510) and (2) fetal alcohol spectrum disorder (FASD; n = 120). Despite higher IQ scores and reading ability, the mTBI group performed significantly worse than the FASD group on all effort indices. Sixteen percent of the mTBI group failed the MSVT, whereas only 5% of the FASD group did. Our findings support the idea that the MSVT measures effort, not ability, in most cases and help to justify incorporating PVTs into pediatric neuropsychological batteries.

Read Full Article
Back to Table of Contents

Hum Brain Mapp. 2015 Mar 17. doi: 10.1002/hbm.22785. [Epub ahead of print]

41. White matter integrity of the cerebellar peduncles as a mediator of effects of prenatal alcohol exposure on eyeblink conditioning.
Fan J, Meintjes EM, Molteno CD, Spottiswoode BS, Dodge NC, Alhamud AA, Stanton ME, Peterson BS, Jacobson JL, Jacobson SW. (South Africa)

ABSTRACT
Fetal alcohol spectrum disorders (FASD) are characterized by a range of neurodevelopmental deficits that result from prenatal exposure to alcohol. These can include cognitive, behavioural, and neurological impairment, as well as structural and functional brain damage. Eyeblink conditioning (EBC) is among the most sensitive endpoints affected in FASD. The cerebellar peduncles, large bundles of myelinated nerve fibers that connect the cerebellum to the brainstem, constitute the principal white matter element of the EBC circuit. Diffusion tensor imaging (DTI) is used to assess white matter integrity in fibre pathways linking brain regions. DTI scans of 54 children with FASD and 23 healthy controls, mean age 10.1 ± 1.0 years, from the Cape Town Longitudinal Cohort were processed using voxelwise group comparisons. Prenatal alcohol exposure was related to lower fractional anisotropy (FA) bilaterally in the superior cerebellar peduncles and higher mean diffusivity (MD) in the left middle peduncle, effects that remained significant after controlling for potential confounding variables. Lower FA and higher MD in these regions were associated with poorer EBC performance. Moreover, effects of alcohol exposure on EBC decreased significantly after inclusion of these DTI measures in regression models, suggesting that these white matter deficits partially
mediate the relation of prenatal alcohol exposure to EBC. The associations of greater alcohol consumption with these DTI measures are largely attributable to greater radial diffusivity, possibly indicating poorer myelination. Thus, these data suggest that fetal alcohol-related deficits in EBC are attributable, in part, to poorer myelination in key regions of the cerebellar peduncles.

Read Full Article

Back to Table of Contents


42. Neuroimaging effects of prenatal alcohol exposure on the developing human brain: a magnetic resonance imaging review.
Donald KA, Eastman E, Howells FM, Adnams C, Riley EP, Woods RP, Narr KL, Stein DJ (USA, South Africa)

ABSTRACT
OBJECTIVE:
This paper reviews the magnetic resonance imaging (MRI) literature on the effects of prenatal alcohol exposure on the developing human brain.

METHOD:
A literature search was conducted through the following databases: PubMed, PsycINFO and Google Scholar. Combinations of the following search terms and keywords were used to identify relevant studies: 'alcohol', 'fetal alcohol spectrum disorders', 'fetal alcohol syndrome', 'FAS', 'FASD', 'MRI', 'DTI', 'MRS', 'neuroimaging', 'children' and 'infants'.

RESULTS:
A total of 64 relevant articles were identified across all modalities. Overall, studies reported smaller total brain volume as well as smaller volume of both the white and grey matter in specific cortical regions. The most consistently reported structural MRI findings were alterations in the shape and volume of the corpus callosum, as well as smaller volume in the basal ganglia and hippocampi. The most consistent finding from diffusion tensor imaging studies was lower fractional anisotropy in the corpus callosum. Proton magnetic resonance spectroscopy studies are few to date, but showed altered neurometabolic profiles in the frontal and parietal cortex, thalamus and dentate nuclei. Resting-state functional MRI studies reported reduced functional connectivity between cortical and deep grey matter structures. Discussion There is a critical gap in the literature of MRI studies inalcohol-exposed children under 5 years of age across all MRI modalities. The dynamic nature of brain maturation and appreciation of the effects ofalcohol exposure on the developing trajectory of the structural and functional network argue for the prioritisation of studies that include a longitudinal approach to understanding this spectrum of effects and potential therapeutic time points.

Read Full Article

Back to Table of Contents


43. Do pediatricians recognize fetal alcohol spectrum disorders in children with developmental and behavioral problems?
Rojmahamongkol P, Cheema-Hasan A, Weitzman C (Thailand)
ABSTRACT

OBJECTIVE:
Limited studies have examined pediatricians’ knowledge, attitudes, and practice about fetal alcohol spectrum disorders (FASDs), and none have examined alcohol-related neurodevelopmental disabilities (ARND). This study examined whether pediatricians consider FASDs in children with developmental and behavioral problems.

METHODS:
All 149 pediatricians, 55 males and 94 females, in New Haven County, CT, were contacted to complete a web-based survey. They were given cases of preschool boys with (1) fetal alcohol syndrome (FAS), (2) ARND, and (3) Williams Syndrome (WS) and asked to provide a diagnosis and rate their confidence in this. They could access up to 7 additional pieces of information.

RESULTS:
Sixty-six pediatricians responded (44.3%), and 46 had complete data (30.9%). Eight (17.4%) correctly identified FAS and 29 (63.1%) ARND. Significantly fewer pediatricians diagnosed FAS versus ARND and WS (p < .001), and they were less confident in identifying FAS and ARND than WS (10.9 % and 45.7% vs. 73.9%, p < .01). After viewing the photographs with sentinel dysmorphology and case description, respondents were more likely to diagnose WS (37%) versus FAS (19.6%) (p = .064), less confident in their diagnosis (p = .009), and required more information to make an FAS diagnosis (p = .002).

CONCLUSIONS:
Pediatricians underrecognize FASDs, lack confidence in making this diagnosis, and are unfamiliar with the diagnostic criteria. They need more training to consider the possibility of an FASD when seeing children with developmental and behavioral problems.

Read Full Article
Back to Table of Contents
including birth records, medical records from child development centers or other specialty clinics, and administrative databases such as hospital discharge and Medicaid. One challenge of FASSNetII was its limited access to non-medical records. The FAS prevalence that could be estimated was that of the population identified through an encounter with the healthcare system. Clinical and public health programs that identify children affected by FAS provide critical information for targeting preventive, medical and educational services in this vulnerable population.

Read Full Article

Back to Table of Contents


Kreitinger C, Gutierrez H, Hamidovic A, Schmitt C, Sarangarm P, Rayburn WF, Leeman L, Bakhireva LN. (USA)

ABSTRACT
OBJECTIVE:
This study examined the effects of prenatal alcohol exposure (PAE) on the incidence and severity of neonatal abstinence syndrome (NAS).

STUDY DESIGN:
For this pilot study, 70 pregnant women on opioid maintenance therapy (OMT) were recruited from a perinatal substance abuse clinic. Subjects were categorized into three study groups based on the timing of alcohol use during pregnancy as assessed by repeated self-reported measures and a comprehensive panel of ethanol biomarkers. NAS outcomes included: duration of hospital stay, the need for pharmacological treatment of NAS, newborn age at the initiation of NAS treatment, duration of treatment and cumulative methadone dose administered.

RESULTS:
The study included a large proportion of ethnic minorities (81.4% Hispanic, 5.7% American Indian), women with less than a high school education (52.2%) and unplanned pregnancy (82.9%). In multivariate analysis, PAE was not associated with NAS outcomes; however, one newborn diagnosed with fetal alcohol syndrome (FAS) demonstrated much more severe NAS compared to other PAE infants. Interestingly, 3rd trimester PAE was associated with a higher prevalence of microcephaly (62.5%) compared to the PAE abstaining group (36.8%; p = 0.08).

CONCLUSION:
In this study, PAE was not associated with NAS severity; however, further examination in a larger study is needed.

Read Full Article
Back to Table of Contents


46. Visual search for feature conjunctions: an fMRI study comparing alcohol-related neurodevelopmental disorder (ARND) to ADHD.
O’Conaill CR, Malisza KL, Buss JL, Bolster RB, Clancy C, de Gervai PD, Chudley AE, Longstaffe S. (Canada)

ABSTRACT
BACKGROUND:
Alcohol-related neurodevelopmental disorder (ARND) falls under the umbrella of fetal alcohol spectrum disorder (FASD). Diagnosis of ARND is difficult because individuals do not
demonstrate the characteristic facial features associated with fetal alcohol syndrome (FAS). While attentional problems in ARND are similar to those found in attention-deficit/hyperactivity disorder (ADHD), the underlying impairment in attention pathways may be different.

METHODS:
Functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) was conducted at 3 T. Sixty-three children aged 10 to 14 years diagnosed with ARND, ADHD, and typically developing (TD) controls performed a single-feature and a feature-conjunction visual search task.

RESULTS:
Dorsal and ventral attention pathways were activated during both attention tasks in all groups. Significantly greater activation was observed in ARND subjects during a single-feature search as compared to TD and ADHD groups, suggesting ARND subjects require greater neural recruitment to perform this simple task. ARND subjects appear unable to effectively use the very efficient automatic perceptual ‘pop-out’ mechanism employed by TD and ADHD groups during presentation of the disjunction array. By comparison, activation was lower in ARND compared to TD and ADHD subjects during the more difficult conjunction search task as compared to the single-feature search. Analysis of DTI data using tract-based spatial statistics (TBSS) showed areas of significantly lower fractional anisotropy (FA) and higher mean diffusivity (MD) in the right inferior longitudinal fasciculus (ILF) in ARND compared to TD subjects. Damage to the white matter of the ILF may compromise the ventral attention pathway and may require subjects to use the dorsal attention pathway, which is associated with effortful top-down processing, for tasks that should be automatic. Decreased functional activity in the right temporoparietal junction (TPJ) of ARND subjects may be due to a reduction in the white matter tract’s ability to efficiently convey information critical to performance of the attention tasks.

CONCLUSIONS:
Limited activation patterns in ARND suggest problems in information processing along the ventral frontoparietal attention pathway. Poor integrity of the ILF, which connects the functional components of the ventral attention network, in ARND subjects may contribute to the attention deficits characteristic of the disorder.

Read Full Article
Back to Table of Contents


47. Alcohol use disorders in pregnancy.
DeVido J, Bogunovic O, Weiss RD. (USA)

ABSTRACT
Alcohol use disorders (AUDs) are less prevalent in pregnant women than in nonpregnant women, but these disorders can create a host of clinical challenges when encountered. Unfortunately, little evidence is available to guide clinical decision making in this population. Drinking alcohol during pregnancy can have negative consequences on both fetus and mother, but it remains controversial as to the volume of alcohol consumption that correlates with these consequences. Likewise, little evidence is available to support the use of particular pharmacologic interventions for AUDs during pregnancy or to guide the management of alcohol detoxification in pregnant women. The use of benzodiazepines (the mainstay of most alcohol detoxification protocols) in pregnant women is controversial. Nevertheless, despite the lack of robust data to guide management of AUDs in pregnancy, clinicians need to make management decisions when confronted with these challenging situations. In that context, this article reviews the epidemiology of AUDs in pregnancy and the pharmacologic management of both AUDs and alcohol withdrawal in pregnant women, with the goal of informing clinicians about what is known about managing these co-occurring conditions.
48. **Docosahexaenoic acid partially ameliorates deficits in social behavior and ultrasonic vocalizations caused by prenatal ethanol exposure.**

Wellmann KA, George F, Brnouti F, Mooney SM. (USA); kwellmann@peds.umaryland.edu, smooney@peds.umaryland.edu

**ABSTRACT**

Prenatal ethanol exposure disrupts social behavior in humans and rodents. One system particularly important for social behavior is the somatosensory system. Prenatal ethanol exposure alters the structure and function of this area. Docosahexaenoic acid (DHA), an omega 3 polyunsaturated fatty acid, is necessary for normal brain development and brains from ethanol-exposed animals are DHA deficient. Thus, we determined whether postnatal DHA supplementation ameliorated behavioral deficits induced by prenatal ethanol exposure. Timed pregnant Long-Evans rats were assigned to one of three groups: ad libitum access to an ethanol-containing liquid diet, pair fed an isocaloric isonutritive non-alcohololiquid diet, or ad libitum access to chow and water. Pups were assigned to one of two postnatal treatment groups; gavaged intragastrically once per day between postnatal day (P)11 and P20 with DHA (10g/kg in artificial rat milk) or artificial rat milk. A third group was left untreated. Isolation-induced ultrasonic vocalizations (iUSVs) were recorded on P14. Social behavior and play-induced USVs were tested on P28 or P42. Somatosensory performance was tested with a gap crossing test around P33 or on P42. Anxiety was tested on elevated plus maze around P35. Animals exposed to ethanol prenatally vocalized less, play fought less, and crossed a significantly shorter gap than control-treated animals. Administration of DHA ameliorated these ethanol-induced deficits such that the ethanol-exposed animals given DHA were no longer significantly different to control-treated animals. Thus, DHA administration may have therapeutic value to reverse some of ethanol's damaging effects.

Read Full Article
Back to Table of Contents

49. **Dose effect of gestational ethanol exposure on placentation and fetal growth.**

Gundogan F1, Gilligan J2, Qi W2, Chen E2, Naram R3, de la Monte SM4. (USA); Suzanne_DeLaMonte_MD@Brown.edu

**ABSTRACT**

**INTRODUCTION:**

Prenatal ethanol exposure compromises fetal growth by impairing placentation. Invasive trophoblastic cells, which mediate placentation, express the insulin-IGF regulated gene, aspartyl-asparaginyl β-hydroxylase (ASPH), which has a critical role in cell motility and invasion. The aims of this study were to characterize effects of ethanol on trophoblastic cell motility, and assess ethanol dose-dependent impairments in placentation and fetal development.

**METHODS:**

Pregnant Long Evans dams were fed with isocaloric liquid diets containing 0%, 8%, 18% or 37% ethanol (caloric content) from gestation day (GD) 6 to GD18. Fetal development, placental morphology, density of invasive trophoblasts at the mesometrial triangle, as well as placental and...
mesometrial ASPH and Notch-1 protein expression were evaluated. Directional motility of control and ethanol-exposed HTR-8/SVneo cells was assessed by ATP Luminescence-Based assay.

RESULTS:
Severity of fetal growth impairment correlated with increasing doses of ethanol. Ethanol exposure produced dose-dependent alterations in branching morphogenesis at the labyrinthine zone, and inhibited physiological transformation of maternal arteries. ASPH and Notch-1 protein expression levels were reduced, corresponding with impairments in placentation.

DISCUSSION:
Prenatal ethanol exposure compromises fetal growth and placentation in a dose-responsive manner. Ethanol's adverse effects on placental development are mediated by: (1) altered branching morphogenesis in labyrinthine zone; (2) suppression of invasive trophoblastic precursor cells; and (3) inhibition of trophoblastic cell adhesion and motility, corresponding with reduced ASPH and Notch-1 protein expression.

Read Full Article
Back to Table of Contents


50. Executive function and cortical thickness in youths prenatally exposed to cocaine, alcohol and tobacco
Gautam P1, Warner TD2, Kan EC1, Sowell ER3. (USA); esowell@chla.usc.edu

ABSTRACT
Small and detrimental, albeit inconsistent, effects of prenatal cocaine exposure (PCE) during early childhood have been reported. The teratogenic effects of prenatal alcohol (PAE) and tobacco exposure (PTE) on neurobehavior are more firmly established than PCE. We tested if co-exposure to all three drugs could be related to greater differences in brain structure than exposure to cocaine alone. Participants (n=42, PCE=27; age range=14-16 years) received an executive function battery prior to a T1-weighted 3T structural MRI scan. Cortical thickness was measured using FreeSurfer (v5.1). Fetal drug exposure was quantified through maternal self-reports usage during pregnancy. Using general linear modeling, we found no main effects of PCE on cortical thickness, but significant main effects of PAE and PTE in superior and medial frontal regions, after co-varying for the effects of age, sex, and each drug of exposure. Significant alcohol-by-tobacco interactions, and significant cocaine-by-alcohol interactions on cortical thickness in medial parietal and temporal regions were also observed. Poly-drug exposure and cognitive function also showed significant interactions with cortical thickness: lower cortical thickness was associated with better performance in PCE-exposed adolescents. Results suggest that although children with PCE have subtle but persistent brain cortical differences until mid-to-late adolescence.

Read Full Article
Back to Table of Contents


51. Maternal L-glutamine supplementation prevents prenatal alcohol exposure-induced fetal growth restriction in an ovine model.
Sawant OB1, Wu G, Washburn SE. (USA)

ABSTRACT
Prenatal alcohol exposure is known to cause fetal growth restriction and disturbances in amino acid bioavailability. Alterations in these parameters can persist into adulthood and low birth weight can
Glutamine has been associated with the synthesis of other amino acids, an increase in protein synthesis and it is used clinically as a nutrient supplement for low birth weight infants. The aim of this study was to explore the effect of repeated maternal alcohol exposure and L-glutamine supplementation on fetal growth and amino acid availability during the third trimester-equivalent period in an ovine model. Pregnant sheep were randomly assigned to four groups, saline control, alcohol (1.75-2.5 g/kg), glutamine (100 mg/kg, three times daily) or alcohol + glutamine. In this study, a weekend binge drinking model was followed where treatment was done 3 days per week in succession from gestational day (GD) 109-132 (normal term ~147). Maternal alcohol exposure significantly reduced fetal body weight, height, length, thoracic girth and brain weight, and resulted in decreased amino acid bioavailability in fetal plasma and placental fluids. Maternal glutamine supplementation successfully mitigated alcohol-induced fetal growth restriction and improved the bioavailability of glutamine and glutamine-related amino acids such as glycine, arginine, and asparagine in the fetal compartment. All together, these findings show that L-glutamine supplementation enhances amino acid availability in the fetus and prevents alcohol-induced fetal growth restriction.

Read Full Article
Back to Table of Contents

52. Diagnosing FASD in adults: the development and operation of an adult FASD clinic in Ontario, Canada.

Temple VK, Ives J, Lindsay A. (Canada)

ABSTRACT
This paper describes the development and operation of an interdisciplinary Fetal Alcohol Spectrum Disorders (FASD) diagnostic clinic focusing specifically on adults. The clinic is embedded within a community-based interdisciplinary health agency specializing in intellectual and developmental disabilities. A review of the clinic’s assessment process is presented describing the steps from intake to feedback and intervention. To date, the clinic has received 93 referrals and given 41 alcohol-related diagnoses including 10 completed using videoconferencing technology. Issues unique to adult diagnosis are discussed as well as some of the challenges, including high rates of cancellations/no-shows for appointments, obtaining background and historical information, establishing maternal alcohol history, working collaboratively with other support sectors such as children’s protective services and the justice system, and finding appropriate follow-up and intervention services in the community. Recommendations for future work to support adults with FASD and their families are presented.

Read Full Article
Back to Table of Contents


53. Maternal alcohol intake around the time of conception causes glucose intolerance and insulin insensitivity in rat offspring, which is exacerbated by a postnatal high-fat diet.

Gårdebjer EM, Anderson ST, Pantaleon M, Włodek ME, Moritz KM. (Australia); k.moritz@uq.edu.au

ABSTRACT
Alcohol consumption throughout pregnancy can cause metabolic dysregulation, including glucose intolerance in progeny. This study determined if periconceptional (PC) alcohol (12% v/v in a liquid diet) (PC:EtOH) consumed exclusively around conception results in similar outcomes in Sprague-Dawley rats. Control (C) rats were given a liquid diet containing no alcohol but matched to ensure equal caloric intake. PC maternal alcohol intake (from 4 days before conception until day 4 of gestation), resulted in offspring with elevated fasting plasma glucose (~10-25%, P < 0.05), impaired
glucose tolerance (P < 0.05), and decreased insulin sensitivity (P < 0.01) at 6 months of age. This was associated with increased hepatic gluconeogenesis and sex-specific alterations in peripheral protein kinase B (AKT) signaling. These changes were accompanied by increased mRNA expression of DNA methyltransferases (DNMTs) 1, 3a, and 3b (1.5- to 1.9-fold, P < 0.05) in fetal liver in late gestation, suggesting PC:EtOH may cause epigenetic changes that predispose offspring to metabolic dysfunction. Exposure to a postnatal (PN) high-fat and cholesterol diet (HFD) from 3 months of age caused hyperinsulinemia (~2-fold increase, P < 0.001) and exacerbated the metabolic dysfunction in male offspring exposed to PC:EtOH but had no additive effects in females. Given many women may drink alcohol while planning a pregnancy, it is crucial to increase public awareness regarding the effects of alcohol consumption around conception on offspring health.

Gårdebjer, E. M., Anderson, S. T., Pantaleon, M., Wlodek, M. E., Moritz, K. M. Maternal alcohol intake around the time of conception causes glucose intolerance and insulin insensitivity in rat offspring, which is exacerbated by a postnatal high-fat diet.

Read Full Article
Back to Table of Contents


ABSTRACT
The adverse effects of maternal alcohol use during pregnancy represent a spectrum of growth restriction, facial dysmorphology, and neurocognitive challenges in the offspring. The continuum of diagnoses is referred to as fetal alcohol spectrum disorders (FASD). Short palpebral fissures, a smooth philtrum, and a thin vermilion border of the upper lip comprise the three cardinal facial features of FASD. Early attempts to define a smooth philtrum and thin vermilion border of the upper lip were subjective. Astley and colleagues introduced a 5-point Likert-scaled lip/philtrum guide based on Caucasian North American subjects as an objective tool for the evaluation of the facial dysmorphology in FASD. This Caucasian guide has been incorporated into all current diagnostic schemes for FASD. However, broad international clinical experience with FASD indicates racial and ethnic differences with respect to the facial morphology. Because of the substantial number of children with FASD in South Africa among the Cape Coloured (mixed race) population in the Western Cape Province, we developed a specific lip/philtrum guide for that population. The guide incorporates a 45-degree view of the philtrum that enables an enhanced 3-dimensional evaluation of philtral height not possible with a frontal view alone. The guide has proven to be a more specific and sensitive tool for evaluation of the facial dysmorphology of FASD in the Cape Coloured population than the use of the previous North American Caucasian guide and points to the utility of racial and ethnic-specific dysmorphology tools in the evaluation of children with suspected FASD.

Read Full Article
Back to Table of Contents


55. Volume changes and brain-behavior relationships in white matter and subcortical gray matter in children with prenatal alcohol exposure.
ABSTRACT
Children with prenatal alcohol exposure (PAE) may have cognitive, behavioral and brain abnormalities. Here, we compare rates of white matter and subcortical gray matter volume change in PAE and control children, and examine relationships between annual volume change and arithmetic ability, behavior, and executive function. Participants (n = 75 PAE/64 control; age: 7.1-15.9 years) each received two structural magnetic resonance scans, ~2 years apart. Assessments included Wechsler Intelligence Scale for Children (WISC-IV), the Child Behavior Checklist and the Behavior Rating Inventory of Executive Function. Subcortical white and gray volumes were extracted for each hemisphere. Group volume differences were tested using false discovery rate (q < 0.05). Analyses examined group-by-age interactions and group-score interactions for correlations between change in volume and raw behavioral scores. Results showed that subjects with PAE had smaller volumes than control subjects across the brain. Significant group-score interactions were found in temporal and parietal regions for WISC arithmetic scores and in frontal and parietal regions for behavioral measures. Poorer cognitive/behavioral outcomes were associated with larger volume increases in PAE, while control subjects generally showed no significant correlations. In contrast with previous results demonstrating different trajectories of cortical volume change in PAE, our results show similar rates of subcortical volume growth in subjects with PAE and control subjects. We also demonstrate abnormal brain-behavior relationships in subjects with PAE, suggesting different use of brain resources. Our results are encouraging in that, due to the stable volume differences, there may be an extended window of opportunity for intervention in children with PAE.

Read Full Article
Back to Table of Contents


56. Hypothalamic-pituitary-adrenal axis and behavioral dysfunction following early binge-like prenatal alcohol exposure in mice.
Wieczorek L, Fish EW, O'Leary-Moore SK, Parnell SE, Sulik KK, (USA); lawieczko@med.unc.edu

ABSTRACT
The range of defects that fall within fetal alcohol spectrum disorder (FASD) includes persistent behavioral problems, with anxiety and depression being two of the more commonly reported issues. Previous studies of rodent FASD models suggest that interference with hypothalamic-pituitary-adrenal (HPA) axis structure and/or function may be the basis for some of the prenatal alcohol (ethanol) exposure (PAE)-induced behavioral abnormalities. Included among the previous investigations are those illustrating that maternal alcohol treatment limited to very early stages of pregnancy (i.e., gestational day [GD]7 in mice; equivalent to the third week post-fertilization in humans) can cause structural abnormalities in areas such as the hypothalamus, pituitary gland, and other forebrain regions integral to controlling stress and behavioral responses. The current investigation was designed to further examine the sequelae of prenatal alcohol insult at this early time period, with particular attention to HPA axis-associated functional changes in adult mice. The results of this study reveal that GD7 PAE in mice causes HPA axis dysfunction, with males and females showing elevated corticosterone (CORT) and adrenocorticotropic hormone (ACTH) levels, respectively, following a 15-min restraint stress exposure. Males also showed elevated CORT levels following an acute alcohol injection of 2.0 g/kg, while females displayed blunted ACTH levels. Furthermore, analysis showed that anxiety-like behavior was decreased after GD7 PAE in female mice, but was increased in male mice. Collectively, the results of this study show that early gestational alcohol exposure in mice alters long-term HPA axis activity and behavior in a sexually dimorphic manner.

The range of defects that fall within fetal alcohol spectrum disorder (FASD) includes persistent behavioral problems, with anxiety and depression being two of the more commonly reported issues. Previous studies of rodent FASD models suggest that interference with hypothalamic-pituitary-adrenal (HPA) axis structure and/or function may be the basis for some of the
prenatal alcohol (ethanol) exposure (PAE)-induced behavioral abnormalities. Included among the previous investigations are those illustrating that maternal alcohol treatment limited to very early stages of pregnancy (i.e., gestational day [GD]7 in mice; equivalent to the third week post-fertilization in humans) can cause structural abnormalities in areas such as the hypothalamus, pituitary gland, and other forebrain regions integral to controlling stress and behavioral responses. The current investigation was designed to further examine the sequelae of prenatal alcohol insult at this early time period, with particular attention to HPA axis-associated functional changes in adult mice. The results of this study reveal that GD7 PAE in mice causes HPA axis dysfunction, with males and females showing elevated corticosterone (CORT) and adrenocorticotropic hormone (ACTH) levels, respectively, following a 15-min restraint stress exposure. Males also showed elevated CORT levels following an acute alcohol injection of 2.0 g/kg, while females displayed blunted ACTH levels. Furthermore, analysis showed that anxiety-like behavior was decreased after GD7 PAE in female mice, but was increased in male mice. Collectively, the results of this study show that early gestational alcohol exposure in mice alters long-term HPA axis activity and behavior in a sexually dimorphic manner.

Read Full Article
Back to Table of Contents


57. Alcohol odor elicits appetitive facial expressions in human neonates prenatally exposed to the drug.
Faas AE, March SM, Moya PR, Molina JC. (Argentina); ana.faas@gmail.com, juancmolina2003@hotmail.com.ar

ABSTRACT
Specific memories arise during prenatal life as a function of fetal processing of chemosensory stimuli present in the amniotic fluid. Preclinical studies indicate that fetal exposure to alcohol modifies subsequent neonatal and infantile responsiveness towards the sensory attributes of the drug. It has been previously demonstrated that 1-2day-old human neonates recognize ethanol odor as a function of moderate maternal alcohol consumption during gestation. In the present study 7-14day-old newborns were assessed in terms of behavioral responsiveness to alcohol's chemosensory attributes or to a novel odor (lemon). These newborns were representative of mothers that exhibited infrequent or frequent alcohol drinking patterns during pregnancy. Different clinical assessments indicated that all newborns did not suffer congenital or genetic diseases and that they were completely healthy when behaviorally evaluated. Testing was defined by brief presentations of ethanol or lemon odorants. Two sequences of olfactory stimulation were employed. One sequence included five initial trials defined by ethanol odor stimulation followed by one trial with lemon and five additional trials with the scent of the drug (EtOH-Lem-EtOH). The alternative sequence (Lem-EtOH-Lem) was primarily defined by lemon olfactory exposure. The dependent variables under analysis were duration and frequency of overall body movements and of facial expressions categorized as aversive or appetitive. The main results of this study were as follows: a) at the end of the testing procedure and independent of the sequence of olfactory stimulation, babies born to frequent drinkers exhibited signs of distress as operationalized through higher durations of aversive facial expressions, b) despite this effect, babies born to frequent drinkers relative to newborns delivered by infrequent drinkers exhibited significantly higher frequencies of appetitive facial responses when primarily stimulated with ethanol odor (EtOH-Lem-EtOH sequence) and c) when merging both samples of babies, a positive and significant correlation was found between overall maternal absolute alcohol consumption per month and frequency of appetitive facial expressions elicited by alcohol odor. In conjunction with previous preclinical research, the present results indicate that human prenatal exposure to the drug that yields no evident teratological effects is sufficient to modify the hedonic value of alcohol's chemosensory attributes.
Kerns KA, Siklos S, Baker L, Müller U. (Canada)

ABSTRACT
There is a limited amount of research that examines social-emotional functioning in children with Fetal Alcohol Spectrum Disorder (FASD), and the majority of it relies on parent and teacher reports of social impairments. Because these provide broad measures of social function, they fail to elucidate the underlying specific skills with which this group of children has difficulty. The current study examines emotion-recognition abilities in children with FASD, as it plays a central role in social interaction. Participants were 22 children with diagnosed FASD (ages 8-14), and age- and gender-matched typically developing controls. Tasks included measures of emotion recognition from three nonlinguistic modalities: facial expressions, emotional tone of voice, and body positioning and movement. Participant’s parents completed measures of adaptive and behavioral function that were related to children’s performance on aspects of emotion recognition. Overall, the results show that children with FASD have more difficulties with emotion recognition than typically developing age-matched peers, but these difficulties may not be clinically significant (e.g., smaller effect size) or may be specific to the age of the individual exhibiting the emotion (i.e., child vs. adult). These results are discussed in the context of previous studies.

59. Fatty acid ethyl esters disrupt neonatal alveolar macrophage mitochondria and derange cellular functioning.
Mohan SS, Ping XD, Harris FL, Ronda NJ, Brown LA, Gauthier TW. (USA)

ABSTRACT
BACKGROUND:
Chronic alcohol exposure alters the function of alveolar macrophages (AM), impairing immune defenses in both adult and neonatal lungs. Fatty acid ethyl esters (FAEEs) are biological markers of prenatal alcohol exposure in newborns. FAEEs contribute to alcohol-induced mitochondrial (MT) damage in multiple organs. We hypothesized that in utero ethanol exposure would increase FAEEs in the neonatal lung and that direct exposure of neonatal AM to FAEEs would contribute to MT injury and cellular dysfunction.

METHODS:
FAEEs were measured in neonatal guinea pig lungs after ± in utero ethanol exposure via gas chromatography/mass spectrometry. The NR8383 cell line and freshly isolated neonatal guinea pig AM were exposed to ethyl oleate (EO) in vitro. MT membrane potential, MT reactive oxygen species generation (mROS), phagocytosis, and apoptosis were evaluated after exposure to EO ± the MT-specific antioxidant mito-TEMPO (mitoT) or ± the pan-caspase inhibitor Z-VAD-FMK. Whole lung FAEEs were compared using the Mann-Whitney U-test. Cellular results were analyzed using 1-way analysis of variance, followed by the Student-Newman-Keuls Method for post hoc comparisons.

RESULTS:
In utero ethanol significantly increased ethyl linoleate and the combinations of ethyl oleate + linoleate + linolenate (OLL), and OLL + stearate in the neonatal lung. In vitro EO caused significant MT dysfunction in both NR8383 and primary neonatal AM, as indicated by increased mROS and loss of MT membrane potential. Impaired phagocytosis and apoptosis were significantly increased in both the cell line and primary AM after EO exposure. MitoT conferred significant but only partial protection against EO-induced MT injury, as did caspase inhibition with Z-VAD-FMK.

CONCLUSIONS:
In utero ethanol exposure increased FAEEs in the neonatal guinea pig lung. Direct exposure to the FAEE EO significantly contributed to AM dysfunction, in part via oxidant injury to the MT and in part via secondary apoptosis.

Read Full Article
Back to Table of Contents

60. Acetaldehyde, not ethanol, impairs myelin formation and viability in primary mouse oligodendrocytes.
Coutts DJ, Harrison NL. (USA)

ABSTRACT
BACKGROUND:
Excessive ethanol (EtOH) drinking is associated with white matter loss in the brain at all stages of life. Myelin-forming oligodendrocytes (OLs) are a major component of white matter, but their involvement in EtOH-mediated white matter loss is unclear. Myelination continues throughout the life with highest rates during fetal development and adolescence. However, little is known about the effects of EtOH and its principal metabolite acetaldehyde (ACD) on OLs at the cellular level.

METHODS:
We compared the responses to different concentrations of EtOH or ACD by primary OLs in culture.

RESULTS:
EtOH did not cause significant cell death at concentrations lower than 120 mM, even after 24 hours. In comparison, ACD was highly lethal at doses above 50 μM. High concentrations of EtOH (120 mM) and ACD (500 μM) for 24 hours did not reduce myelin in mature OLs. Myelin production and OL differentiation were significantly impaired by 7 days exposure to 500 or 50 μM ACD but not 120 mM EtOH.

CONCLUSIONS:
This study shows that OLs are relatively resistant to EtOH, even at a concentration more than 4 times the typical blood EtOH concentrations associated with social drinking (10 to 30 mM). In contrast, OLs are much more sensitive to ACD than EtOH, particularly with long-term exposure. This suggests that part of white matter loss in response to EtOH, especially during high rates of myelin formation, may be due in part to the effects of its principal metabolite ACD.

Read Full Article
Back to Table of Contents

Drew PD, Johnson JW, Douglas JC, Phelan KD, Kane CJ. (USA)

ABSTRACT

BACKGROUND:

Fetal alcohol spectrum disorders (FASD) result from fetal exposure to alcohol and are the leading cause of mental retardation in the United States. There is currently no effective treatment that targets the causes of these disorders. Thus, novel therapies are critically needed to limit the neurodevelopmental and neurodegenerative pathologies associated with FASD.

METHODS:

A neonatal mouse FASD model was used to examine the role of the neuroimmune system in ethanol (EtOH)-induced neuropathology. Neonatal C57BL/6 mice were treated with EtOH, with or without pioglitazone, on postnatal days 4 through 9, and tissue was harvested 1 day post treatment. Pioglitazone is a peroxisome proliferator-activated receptor (PPAR)-γ agonist that exhibits anti-inflammatory activity and is neuroprotective. We compared the effects of EtOH with or without pioglitazone on cytokine and chemokine expression and microglial morphology in the hippocampus, cerebellum, and cerebral cortex.

RESULTS:

In EtOH-treated animals compared with controls, cytokines interleukin-1β and tumor necrosis factor-α mRNA levels were increased significantly in the hippocampus, cerebellum, and cerebral cortex. Chemokine CCL2 mRNA was increased significantly in the hippocampus and cerebellum. Pioglitazone effectively blocked the EtOH-induced increase in the cytokines and chemokine in all tissues to the level expressed in handled-only and vehicle-treated control animals. EtOH also produced a change in microglial morphology in all brain regions that was indicative of microglial activation, and pioglitazone blocked this EtOH-induced morphological change.

CONCLUSIONS:

These studies indicate that EtOH activates microglia to a pro-inflammatory stage and also increases the expression of proinflammatory cytokines and chemokines in diverse regions of the developing brain. Further, the anti-inflammatory and neuroprotective PPAR-γ agonist pioglitazone blocked these effects. It is proposed that microglial activation and inflammatory molecules expressed as a result of EtOH treatment during brain development contribute to the sequelae associated with FASD. Thus, pioglitazone and anti-inflammatory pharmaceuticals more broadly have potential as novel therapeutics for FASD.

Read Full Article
Back to Table of Contents


Mandal C, Park JH, Choi MR, Kim SH, Badejo AC, Chai JC, Lee YS, Jung KH, Chai YG. (Republic of Korea)

ABSTRACT

Neural stem cells (NSCs) can be differentiated into one of three cell lineages: neurons, astrocytes or, oligodendrocytes. Some neurotoxins have the ability to deregulate this dynamic process. NSC cell fate can be altered by ethanol as reported previously. Our aim was to investigate the alteration
of genes by ethanol during NSC differentiation and to explore the molecular mechanism underlying this phenomenon. Here, mouse fetal forebrain derived NSCs were differentiated for 2 days with or without of ethanol (50 mM). We performed a comparative microarray analysis at day two using GeneChip® Mouse Genome 430A 2.0 arrays. Microarray analysis showed that the expressions of 496 genes were altered by ethanol (56 and 440 were up- and down-regulated, respectively). Kyoto Encyclopedia of Genes and Genomes pathway analysis revealed the association of the following altered genes in the Wnt signaling pathway: Wnt5a, Csnk2a1, Tcf7l2, Ccnd2, Nlk, Tbl1x, Tbl1xr1, Rac2 and Nfatc3. Quantitative real time PCR analysis also demonstrated the relative expression levels of these genes. As Wnt signaling is a player of brain development, ethanol-induced alterations may contribute to improper development of the brain. Our data could be a useful resource for elucidating the mechanism behind the ethanol neurotoxicity in developing brain.

Read Full Article

Back to Table of Contents


63. Cognitive and executive functions, social cognition and sense of coherence in adults with fetal alcohol syndrome.
Rangmar J, Sandberg AD, Aronson M, Fahlke C. (Sweden)

ABSTRACT
Background: Primary disabilities in children with fetal alcohol syndrome (FAS) are the results of alcohol’s teratogen effect on the fetal brain. Reduced cognitive and executive functions and social cognition are examples of such disabilities. Little is known about primary disabilities in adults with FAS as well as their sense of coherence (SoC). There is thus a need for knowledge about FAS in adulthood. Aims: To investigate cognitive and executive functions, social cognition and SoC in adults with FAS. Methods: Twenty adults with FAS (mean age: 30 years) were compared with 20 individuals matched on gender and age. Berg's Card-sorting Test-64, the Tower of Hanoi, Raven's Coloured Progressive Matrices, Digit Span, Faux Pas and the Swedish version of Antonovsky's Sense of Coherence Scale (SoC-29) were used. Results: The FAS group had a weak SoC and displayed deficits in the neuropsychological tests sensitive to cognitive and executive functions and social cognition. The FAS group's median SoC score was 112, lower than the comparison group's median of 133 (P < 0.001). The FAS group had median scores of 29.0 on Raven's Matrices. The median for Digit Span was 5 forwards and 3 backwards, lower than in the comparison group (P < 0.001). Conclusions: Reduced cognitive and executive functions and impaired social cognition are assumed to have a major impact on life for adults with FAS. We suggest that the findings showing that adults with FAS had a weak SoC, with particularly low scores on the manageability scale, reflect their experiences of living with those primary disabilities. Clinical implications: This study may enhance healthcare for individuals prenatally exposed to alcohol. In general, it contributes with knowledge about this group of individuals who need to be more visible in healthcare, and particularly, it demonstrates some of the neuropsychological disabilities they might have.

Read Full Article

Back to Table of Contents


64. Prevalence and patterns of alcohol use in pregnancy in remote Western Australian communities: The Liliwan Project.
Fitzpatrick JP, Latimer J, Ferreira ML, Carter M, Oscar J, Martiniuk AL, Watkins RE, Elliott EJ. (Australia)
ABSTRACT
INTRODUCTION AND AIMS:
Alcohol use in pregnancy is thought to be common in remote Australian communities, but no population-based data are available. Aboriginal leaders in remote Western Australia invited researchers to determine the prevalence and patterns of alcohol use in pregnancy within their communities.

DESIGN AND METHODS:
A population-based survey of caregivers of all children born in 2002/2003 and living in the Fitzroy Valley in 2010/2011 (n = 134). Alcohol use risk was categorised using the Alcohol Use Disorders Identification Test consumption subset (AUDIT-C) tool. Birth and child outcomes were determined by interview, medical record review and physical examination.

RESULTS:
127/134 (95%) eligible caregivers participated: 78% were birth mothers, 95% were Aboriginal and 55% reported alcohol use in index pregnancies; 88% reported first trimester drinking and 53% drinking in all trimesters. AUDIT-C scores were calculated for 115/127 women, of whom 60 (52%) reported alcohol use in pregnancy. Of the 60 women who drank (AUDIT-C score ≥ 1), 12% drank daily/almost daily, 33% drank 2-3 times per week; 71% drank ≥10 standard drinks on a typical occasion; 95% drank at risky or high-risk levels (AUDIT-C score ≥ 4). Mean AUDIT-C score was 8.5 ± 2.3 (range 2-12). The most common drinking pattern was consumption of ≥10 standard drinks either 2-4 times per month (27%) or 2-3 times per week (27%).

DISCUSSION AND CONCLUSIONS:
High-risk alcohol use in pregnancy is common in remote, predominantly Aboriginal communities in north western Australia. Prevention strategies to reduce prenatal alcohol use are urgently needed.

Read Full Article
Back to Table of Contents


65. Lifestyle, pregnancy and epigenetic effects.
Barua S1, Junaid MA. (USA)

ABSTRACT
Rapidly growing evidences link maternal lifestyle and prenatal factors with serious health consequences and diseases later in life. Extensive epidemiological studies have identified a number of factors such as diet, stress, gestational diabetes, exposure to tobacco and alcohol during gestation as influencing normal fetal development. In light of recent discoveries, epigenetic mechanisms such as alteration of DNA methylation, chromatin modifications and modulation of gene expression during gestation are believed to possibly account for various types of plasticity such as neural tube defects, autism spectrum disorder, congenital heart defects, oral clefts, allergies and cancer. The purpose of this article is to review a number of published studies to fill the gap in our understanding of how maternal lifestyle and intrauterine environment influence molecular modifications in the offspring, with an emphasis on epigenetic alterations. To support these associations, we highlighted laboratory studies of rodents and epidemiological studies of human based on sampling population cohorts.

Read Full Article
Back to Table of Contents
Karacay B1, Bonthius NE, Plume J, Bonthius DJ. (USA)

ABSTRACT
BACKGROUND:
Alcohol abuse during pregnancy often induces neuropsychological problems in the offspring, including learning disorders, attention deficits, and behavior problems, all of which are prominent components of fetal alcohol spectrum disorders (FASD). However, not all children who were exposed to alcohol in utero are equally affected by it. While some children have major deficits, others are spared. This unequal vulnerability is likely due largely to differences in fetal genetics. Some fetuses appear to have certain genotypes that make them much more prone to FASD. However, to date, no gene has been identified that worsens alcohol-induced brain dysfunction. Nitric oxide (NO) is a gaseous molecule that can protect developing neurons against alcohol-induced death. In the brain, NO is produced by neuronal nitric oxide synthase (nNOS). In this study, we examined whether homozygous mutation of the nNOS gene in mice worsens the behavioral deficits of developmental alcohol exposure.

METHODS:
Wild-type and nNOS(-/-) mice received alcohol (0.0, 2.2, or 4.4 mg/g) daily over postnatal days (PDs) 4 to 9. Beginning on PD 85, the mice underwent a series of behavioral tests, including open field activity, the Morris water maze, and paired pulse inhibition.

RESULTS:
For the wild-type mice, alcohol impaired performance only in the water maze. In contrast, for the nNOS(-/-) mice, alcohol impaired performance on all 3 tasks. Furthermore, the nNOS(-/-) mice were substantially more impaired than wild-type mice in their performance on all 3 of the behavioral tests and at both the low (2.2) and high (4.4) doses of alcohol.

CONCLUSIONS:
Targeted disruption of the nNOS gene worsens the behavioral impact of developmental alcohol exposure and allows alcohol-induced learning problems to emerge that are not seen in wild type. This is the first demonstration that a specific genotype can interact with alcohol to worsen functional brain deficits in an animal model of FASD.

Read Full Article
Back to Table of Contents

67. The neuronal nitric oxide synthase (nNOS) gene and neuroprotection against alcohol toxicity.
Karaçay B, Bonthius DJ. (USA)

ABSTRACT
When a mother abuses alcohol during pregnancy, the offspring can suffer a myriad of abnormalities, collectively known as fetal alcohol spectrum disorder (FASD). Foremost among these abnormalities is central nervous system dysfunction, which commonly manifests itself as mental retardation, clumsiness, hyperactivity, and poor attention span. These behavior problems are due, in large part, to alcohol-induced neuronal losses in the developing fetal brain. However, not all fetuses are equally affected by maternal alcohol consumption during pregnancy. While some fetuses are severely affected and develop hallmarks of FASD later in life, others exhibit no evident neuropathology or
behavioral abnormalities. This variation is likely due, at least in part, to differences in fetal genetics. This review focuses on one particular gene, neuronal nitric oxide synthase, whose mutation worsens alcohol-induced neuronal death, both in vitro and in vivo. In addition, ectopic expression of the neuronal nitric oxide synthase gene protects neurons against alcohol toxicity. The gene encodes an enzyme that produces nitric oxide (NO), which facilitates the protective effects of neuronal growth factors and which underlies the ability of neurons to resist alcohol toxicity as they mature. Nitric oxide exerts its protective effects against alcohol via a specific signaling pathway, the NO-cGMP-PKG pathway. Pharmacologic manipulation of this pathway could be of therapeutic use in preventing or ameliorating FASD.

Read Full Article
Back to Table of Contents


68. [Alcohol and pregnancy: advantage of a screening questionnaire -- a population study].
Lherault S, Chauleur C. (France) [Article in French]

ABSTRACT
INTRODUCTION:
Foetal consequences of an alcoholic exposure in utero may vary according to the intensity of that exposure. A dose-threshold below which alcohol consumption by a pregnant woman would be harmless has not been highlighted. In spite of the recommendations of total abstinence, women's percentage declaring a posteriori to have had a contact with alcohol during pregnancy remains relatively high. We intended to estimate the performance of an auto-questionnaire for the screening of these consumptions. This questionnaire also had to assess the information received by the women about the dangers to consume alcohol during pregnancy.

METHOD:
The questionnaire was distributed to 500 patients in the obstetric consultations of two hospitals.

RESULTS:
63.4% of questionnaires were returned to us; 6.3% of the patients declared an alcohol consumption during pregnancy; 77% considered themselves as sufficiently informed about the question and more than half quoted the healthcare professionals as the information source. The satisfaction as for the received information was significantly connected to behaviour of reducing or giving up the alcohol consumption.

DISCUSSION:
The representativeness of the sample is good with characteristics close to the general population. The sensibility of our questionnaire is superior to that of the standard obstetric interview but stays below the a posteriori evaluations (perinatal investigation). The recommendation of abstinence and the reasons of this recommendation remain relatively underestimated by the general public. The accent should consequently be put on prevention and systematic information.

Read Full Article
Back to Table of Contents


69. Effect of boric acid on oxidative stress in rats with fetal alcohol syndrome.
Sogut I, Oglakci A, Kartkaya K, OI KK, Sogut MS, Kanbak G, Inal ME. (Turkey)

www.nofas-uk.org 109
ABSTRACT
To the best of our knowledge, this is the first study concerning the effect of boric acid (BA) administration on fetal alcohol syndrome (FAS). In this study, the aim was to investigate prenatal alcohol-induced oxidative stress on the cerebral cortex of newborn rat pups and assess the protective and beneficial effects of BA supplementation on rats with FAS. Pregnant rats were divided into three groups, namely the control, alcohol and alcohol + boric acid groups. As markers of alcohol-induced oxidative stress in the cerebral cortex of the newborn pups, malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) levels were measured. Although the MDA levels in the alcohol group were significantly increased compared with those in the control group (P<0.05), the MDA level in the alcohol + boric acid group was shown to be significantly decreased compared with that in the alcohol group (P<0.01). The CAT activity of the alcohol + boric acid group was significantly higher than that in the alcohol group (P<0.05). The GPx activity in the alcohol group was decreased compared with that in the control group (P<0.05). These results demonstrate that alcohol is capable of triggering damage to membranes of the cerebral cortex of rat pups and BA could be influential in antioxidant mechanisms against oxidative stress resulting from prenatal alcohol exposure.

Read Full Article
Back to Table of Contents

70. Genetic absence of nNOS worsens fetal alcohol effects in mice. II: microencephaly and neuronal losses.
Karacay B, Mahoney J, Plume J, Bonthius DJ. (USA)

ABSTRACT
BACKGROUND:
Prenatal alcohol exposure can kill developing neurons, leading to microencephaly and mental retardation. However, not all fetuses are equally vulnerable to alcohol's neurotoxic effects. While some fetuses are severely affected and are ultimately diagnosed with fetal alcohol syndrome (FAS), others have no evidence of neuropathology and are behaviorally normal. These widely different outcomes among alcohol-exposed fetuses are likely due, in part, to genetic differences. Some fetuses possess genotypes that make them much more vulnerable than others to alcohol's teratogenic effects. However, to date, only 1 gene has been identified whose mutation can worsen alcohol-induced behavioral deficits in an animal model of FAS. That gene is neuronal nitric oxide synthase (nNOS). The purpose of this study was to determine whether mutation of nNOS can likewise worsen alcohol-induced microencephaly and lead to permanent neuronal deficits.

METHODS:
Wild-type and nNOS(-/-) mice received alcohol (0.0, 2.2, or 4.4 mg/g) daily over postnatal days (PDs) 4 to 9. Beginning on PD 85, the mice underwent a series of behavioral tests; the results of which are reported in the companion paper. The brains were then weighed, and stereological cell counts were performed on the cerebral cortex and hippocampal formation, which are the brain regions that mediate the aforementioned behavioral tasks.

RESULTS:
Alcohol caused dose-dependent microencephaly, but only in the nNOS(-/-) mice and not in wild-type mice. Alcohol-induced neuronal losses were more severe in the nNOS(-/-) mice than in the wild-type mice in all of the brain regions examined, including the cerebral cortex, hippocampal CA3 subregion, hippocampal CA1 subregion, and dentate gyrus.

CONCLUSIONS:
Targeted mutation of the nNOS gene increases the vulnerability of the developing brain to alcohol-induced growth restriction and neuronal losses. This increased neuropathology is associated with
worsened behavioral dysfunction. The results demonstrate the critical importance of genotype in determining the outcome of developmental alcohol exposure.

Read Full Article
Back to Table of Contents


71. Endogenous opioids as substrates for ethanol intake in the neonatal rat: The impact of prenatal ethanol exposure on the opioid family in the early postnatal period.
Bordner K, Deak T. (USA); bordnerk2@southernct.edu

ABSTRACT
BACKGROUND:
Despite considerable knowledge that prenatal ethanol exposure can lead to devastating effects on the developing fetus, alcohol consumption by pregnant women remains strikingly prevalent. Both clinical and basic research has suggested that, in addition to possible physical, behavioral, and cognitive deficits, gestational exposure to alcohol may lead to an increased risk for the development of later alcohol-related use and abuse disorders. The current work sought to characterize alterations in endogenous opioid signaling peptides and gene expression produced by ethanol exposure during the last days of gestation.

METHODS:
Experimental subjects were 4-, 8-, and 12-day old infant rats obtained from pregnant females that were given daily intubations of 0, 1, or 2g/kg ethanol during the last few days of gestation (GDs 17-20). Using real-time RT-PCR, western blotting analysis, and enzyme immunoassays, we examined mRNA and protein for three opioid receptors and ligands in the nucleus accumbens, ventral tegmental area, and hypothalamus.

RESULTS:
Three main trends emerged - (1) mRNA for the majority of factors was found to upregulate across each of the three postnatal ages assessed, indicative of escalating ontogenetic expression of opioid-related genes; (2) prenatal ethanol significantly reduced many opioid peptides, suggesting a possible mechanism by which prenatal exposure can affect future responsiveness towards ethanol; and (3) the nucleus accumbens emerged as a key site for ethanol-dependent effects, suggesting a potential target for additional assessment and intervention towards understanding the ethanol's ability to program the developing brain.

CONCLUSION:
We provide a global assessment of relatively long-term changes in both opioid gene expression and protein following exposure to only moderate amounts of ethanol during a relatively short window in the prenatal period. These results suggest that, while continuing to undergo ontogenetic changes, the infant brain is sensitive to prenatal ethanol exposure and that such exposure may lead to relatively long-lasting changes in the endogenous opioid system within the reward circuitry. These data indicate a potential mechanism and target for additional assessments of ethanol's ability to program the brain, affecting later responsiveness towards the drug.

Read Full Article
Back to Table of Contents
72. Screening for fetal alcohol spectrum disorders by nonmedical community workers.
O’Connor MJ, Rotheram-Borus MJ, Tomlinson M, Bill C, LeRoux IM, Stewart J. (South Africa)

ABSTRACT
BACKGROUND:
South Africa has the highest prevalence of Fetal Alcohol Spectrum Disorders (FASD) in the world yet many women have no access to clinic care or to physicians in their communities. The shortage of physicians trained in the diagnosis of FASD is even more severe. Thus there is a need to train community workers to assist in the delivery of health care.

OBJECTIVES:
This study reports on the effectiveness of training community workers to screen for a possible diagnosis of a FASD.

METHODS:
Community workers in Cape Town, South Africa were trained to screen for FASD in 139, 18-month-old toddlers with prenatal alcohol exposure (PAE). Children were assessed according to the salient characteristics of individuals with PAE using height, weight, head circumference (OFC), philtrum, and lip measurements according to criteria set forth by the Institute of Medicine. Screen-positive children were referred for diagnostic assessment to a pediatrician reliably trained in the diagnosis of FASD.

RESULTS:
Of the screen-positive children, 93% received an FASD diagnosis suggesting that the screening procedure was highly sensitive. Diagnoses included 15% with fetal alcohol syndrome (FAS), 23% with Partial FAS, and 62% with Alcohol Related Neurodevelopmental Disorder (ARND, provisional).

CONCLUSION:
The use of community workers to screen for FASD represents a promising approach to effective diagnosis of children affected by PAE in areas lacking adequate medical resources.

Read Full Article

Back to Table of Contents


73. A study of the effects of prenatal alcohol exposure on white matter microstructural integrity at birth.
Donald KA, Roos A, Fouche JP, Koen N, Howells FM, Woods RP, Zar HJ, Narr KL, Stein DJ. (South Africa)

ABSTRACT
BACKGROUND:
Neuroimaging studies have indicated that prenatal alcohol exposure is associated with alterations in the structure of specific brain regions in children. However, the temporal and regional specificity of such changes and their behavioural consequences are less known. Here we explore the integrity of regional white matter microstructure in infants with in utero exposure to alcohol, shortly after birth.

METHODS:
Twenty-eight alcohol-exposed and 28 healthy unexposed infants were imaged using diffusion tensor imaging sequences to evaluate white matter integrity using validated tract-based spatial statistics analysis methods. Second, diffusion values were extracted for group comparisons by regions of interest. Differences in fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity were compared between groups and associations with measures from the Dubowitz neonatal neurobehavioural assessment were examined.

www.nofas-uk.org
RESULTS:
Lower AD values (p<0.05) were observed in alcohol-exposed infants in the right superior longitudinal fasciculus compared with non-exposed infants. Altered FA and MD values in alcohol-exposed neonates in the right inferior cerebellar were associated with abnormal neonatal neurobehaviour.

CONCLUSION:
These exploratory data suggest that prenatal alcohol exposure is associated with reduced white matter microstructural integrity even early in the neonatal period. The association with clinical measures reinforces the likely clinical significance of this finding. The location of the findings is remarkably consistent with previously reported studies of white matter structural deficits in older children with a diagnosis of foetal alcohol spectrum disorders.

Read Full Article

Back to Table of Contents


74."If you can have one glass of wine now and then, why are you denying that to a woman with no evidence": Knowledge and practices of health professionals concerning alcohol consumption during pregnancy.
Crawford-Williams F1, Steen M2, Esterman A1, Fielder A2, Mikocka-Walus A3. (Australia); crafm002@mymail.unisa.edu.au

ABSTRACT
BACKGROUND:
Alcohol consumption during pregnancy has the potential to cause significant harm to the foetus and the current Australian guidelines state that it is safest not to drink alcohol while pregnant. However, conflicting messages often appear in the media and it is unclear if the message to avoid alcohol is being effectively conveyed to pregnant women.

AIMS:
This research aims to explore the advice that health professionals provide to pregnant women about alcohol consumption; the knowledge of health professionals regarding the effects of alcohol consumption; and their consistency with following the Australian guidelines.

METHODS:
Ten semi-structured face to face interviews were conducted with health professionals who regularly provide antenatal care. These include midwives, obstetricians, and shared care general practitioners. A six-stage thematic analysis framework was used to analyse the interview data in a systematic way to ensure rigour and transparency. The analysis involved coding data extracts, followed by identifying the major themes.

FINDINGS:
Health professionals displayed adequate knowledge that alcohol can cause physical and mental difficulties that are lifelong; however, knowledge of the term FASD and the broad spectrum of difficulties associated with alcohol consumption during pregnancy was limited. Although health professionals were willing to discuss alcohol with pregnant women, many did not make this a routine part of practice, and several concerning judgements were noted.

CONCLUSION:
Communication between health professionals and pregnant women needs to be improved to ensure that accurate information about alcohol use in pregnancy is being provided. Further, it is important to ensure that the national guidelines are being supported by health professionals.
75. "My midwife said that having a glass of red wine was actually better for the baby": a focus group study of women and their partner's knowledge and experiences relating to alcohol consumption in pregnancy.

Crawford-Williams F1, Steen M2, Esterman A3, Fielder A4, Mikocka-Walus A5,6. (Australia, UK);
crafm002@mymail.unisa.edu.au, antonina.mikocka-walus@york.ac.uk, adrian.esterman@unisa.edu.au,
andrea.fielder@unisa.edu.au

ABSTRACT
BACKGROUND:
While it is well established that alcohol can cross the placenta to the foetus and can affect an infant's development, many women continue to drink during pregnancy. For this reason it is important to determine what information is being provided, what information may be missing, and the preferred sources of information on this issue. In order to improve prevention strategies, we sought to understand the knowledge and experiences of pregnant women and their partners regarding the effects of alcohol consumption during pregnancy.

METHODS:
The current study utilised a qualitative study design in order to gain insight into the views and experiences of pregnant women, newly delivered mothers and their partners. Focus groups examined the participant's knowledge about the effects of alcohol consumption during pregnancy, the sources of information on this issue, and the psycho-social influences on their drinking behaviour. Five focus groups were conducted involving a total of 21 participants (17 female). A six-stage thematic analysis framework was used to analyse all focus group discussions in a systematic way.

RESULTS:
Seven major themes were identified from the focus group data: 1) knowledge of Foetal Alcohol Spectrum Disorders; 2) message content and sources; 3) healthcare system; 4) society and culture; 5) partner role; 6) evaluation of risk; and 7) motivation. The findings indicated that although the majority of participants knew not to drink alcohol in pregnancy they had limited information on the specific harmful effects. In addition, routine enquiry and the provision of information by health care professionals were seen as lacking.

CONCLUSIONS:
The findings of this research provide important insights into the relationship between pregnant women, their partners, and their healthcare providers. Several recommendations can be made on the basis of these findings. Firstly, public health messages and educational materials need to provide clear and consistent information about the effects of alcohol consumption on the developing baby. Additionally, more thorough and consistent routine enquiry for alcohol consumption in pregnant women needs to occur. Finally, it is important to ensure ongoing education for health professionals on the issue of alcohol consumption during pregnancy.

Read Full Article

Back to Table of Contents
76. Children adopted from Poland display a high risk of foetal alcohol spectrum disorders and some may go undiagnosed.

Knuiman S, Rijk CH, Hoksbergen RA, van Baar AL. (The Netherlands)

ABSTRACT

AIM:
Children adopted from Central and Eastern Europe have often had negative early experiences, including prenatal exposure to alcohol. We examined a group of Polish children, adopted by Dutch parents, to see how many were diagnosed with foetal alcohol spectrum disorders (FASD) and to what extent features of FASD were present.

METHODS:
The 121 children, aged between 6 and 17 years, were adopted from Poland at a mean age of 3 years (standard deviation 1.6 years). Their parents answered a questionnaire regarding FASD diagnosis, growth, educational attainment and the Behaviour Rating Inventory of Executive Function.

RESULTS:
Three groups were identified: children with an FASD diagnosis (31%), children whose adoptive parents suspected FASD (21%) and children whose adoptive parents did not suspect FASD (49%). Growth deficiency, enrolment in special education and difficulties with executive functioning were most frequently observed in children diagnosed with FASD. However, features of FASD were also observed in the other two groups.

CONCLUSION:
Children adopted from Poland showed a high risk of FASD and some children may go undiagnosed. Adoptive parents and professionals need to be aware of the potential consequences of prenatal exposure to alcohol.

Read Full Article
Back to Table of Contents

77. What does the general public in the UK know about the risk to a developing foetus if exposed to alcohol in pregnancy? Findings from a UK mixed methodology study.

Mukherjee R, Wray E, Hollins S, Curfs L. (UK)

ABSTRACT

INTRODUCTION:
Foetal alcohol spectrum disorders (FASD) are a set of preventable conditions where the foetus is exposed to alcohol in utero and as a result suffers adverse consequences. To develop a public health strategy related to FASD, it is important to first establish what is known by the public about this condition. This study aimed to assess the current level of knowledge about FASD in the UK general population.

METHODS:
A mixed methodology study was conducted using a 17-item questionnaire and focus group sessions. Four focus groups were held with an average of 10 people in each group. Semi-structured questions and thematic analysis of interviews alongside quantitative analysis of the questionnaire
The research was approved by an National Health service (NHS) research ethical committee.

RESULTS:
A total of 674 people responded to the questionnaire and a majority (86.7%) had heard about FASD, with most receiving their information from the media (26.2%) or from their work (27.7%). Four broad themes emerged. Overall these were: a general lack of knowledge about the subject; information about the subject needed to be personally relevant; there was a need for further education; and there was a lack of clarity in the current guidance on alcohol use in pregnancy.

DISCUSSION AND CONCLUSIONS:
Currently there appears to be a superficial level of knowledge about FASD in the UK general public. More detailed work in subgroups, such as young women, to identify their specific needs may be necessary before targeted public health and educational interventions can be developed to meet the needs of the general public.

Read Full Article
Back to Table of Contents


78. Effects of all three trimester moderate binge alcohol exposure on the foetal hippocampal formation and olfactory bulb.
Washburn SE, Ramadoss J, Chen WJ, Cudd TA. (USA)

ABSTRACT

OBJECTIVE:
Pre-natal alcohol exposure results in injury to the hippocampus and olfactory bulb, but currently there is no consensus on the critical window of vulnerability. This study tested the hypothesis that pre-natal exposure to a moderate dose of alcohol during all three trimester-equivalents alters development of the hippocampal formation and olfactory bulb in an ovine model, where all brain development occurs pre-natally as it does in humans.

RESEARCH DESIGN AND METHODS:
Pregnant sheep were divided into saline control and a binge drinking groups (alcohol dose 1.75 g kg-1; mean peak blood alcohol concentration 189 + 19 mg dl-1).

OUTCOME AND RESULTS:
The density, volume and total cell number were not different between groups for the dentate gyrus, pyramidal cells in the CA1 and CA2/3 fields and mitral cells in the olfactory bulb.

CONCLUSIONS:
A moderate dose of alcohol administered in a binge pattern throughout gestation does not alter cell numbers in the hippocampus or olfactory bulb and exposure during the third trimester-equivalent is required for hippocampal injury, unless very high doses of alcohol are administered. This has important implications in establishing the sensitivity of imaging modalities such as MRI in which volumetric measures are being studied as biomarkers for pre-natal alcohol exposure.

Read Full Article
Back to Table of Contents
79. Prenatal ethanol exposure and placental hCG and IGF2 expression.
Joya X, Salat-Batlle J, Velezmoro-Jáuregui G, Clavé S, Garcia-Algar O, Vall O. (Spain);
90458@hospitaldelmar.cat

ABSTRACT
INTRODUCTION:
Fetal alcohol spectrum disorder (FASD) is the main cause of preventable non-genetic mental retardation. Diagnosis of prenatal exposure to ethanol (PEE) is based on questionnaires and biomarkers in perinatal matrices. Early diagnosis of FASD is important to mitigate secondary disabilities that will arise later in life. It is important to identify biomarkers related to cellular damage caused by PEE. The main objective was to identify novel candidate biomarkers related to cellular damage caused by PEE using an in vitro model of exposure to ethanol and to support it in placental tissue obtained from pregnancies with PEE assessed by fatty acid esters in meconium samples.

METHODS:
First, hormone production was examined using two different human trophoblast cell lines, JEG3 and BeWo. Viable cell count by exclusion method was analyzed and human chorionic gonadotrophin (hCG) and insulin-like growth factor 2 (IGF2) were quantified by Western blot and ELISA. Second, these techniques were used in protein lysates from human placentas from pregnancies with and without exposure to ethanol.

RESULTS:
Both trophoblast cell lines showed a decrease in cell viability accompanied with apoptosis activation after a chronic ethanol treatment. Moreover, we showed an increase in the secretion of hCG and IGF2 in a dose-dependent manner. Interestingly, this increase was also observed in a set of human placenta tissue from fetuses exposed prenatally to ethanol.

DISCUSSION:
Ethanol exposure during pregnancy causes placenta cell damage, so altering its normal function. The specific hCG and IGF2 release pattern is a candidate surrogated biomarker of the damage due to PEE.

Read Full Article
Back to Table of Contents

Ornoy A, Weinstein-Fudim L, Ergaz Z. (Israel); ornoy@cc.huji.ac.il

ABSTRACT
Autism spectrum disorder (ASD) affecting about 1% of all children is associated, in addition to complex genetic factors, with a variety of prenatal, perinatal and postnatal etiologies. We discuss the known associated prenatal factors affecting the fetus throughout pregnancy; whenever relevant, also summarize some animal data. Among the maternal diseases in pregnancy associated with ASD are pregestational and/or gestational diabetes mellitus (PGDM, GDM), maternal infections (i.e. rubella, cytomegalovirus (CMV)), prolonged fever and maternal inflammation, which cause changes in a variety of inflammatory cytokines. Among the drugs are valproic acid, thalidomide, and possibly misoprostol and serotonin reuptake inhibitors (SSRIs). Associations were described with ethanol, and possibly cocaine heavy metals heavy smoking, and Folic acid deficiency. Heavy exposure to pesticides and air pollution during pregnancy was recently associated with ASD. We need more epidemiologic data to establish many of these associations; if proven, they might be promising avenues for prevention.
**ABSTRACT**

Clinical studies demonstrate frequent co-existence of nicotine and alcohol abuse and suggest that this may result, in part, from the ready access to and intake of fat-rich diets. Whereas animal studies show that high-fat diet intake in adults can enhance the consumption of either nicotine or ethanol and that maternal consumption of a fat-rich diet during pregnancy increases operant responding for nicotine in offspring, little is known about the impact of dietary fat on the co-abuse of these two drugs. The goal of this study was to test in Long-Evans rats the effects of perinatal exposure to fat on the co-use of nicotine and ethanol, using a novel paradigm that involves simultaneous intravenous (IV) self-administration of these two drugs. Fat- vs. chow-exposed offspring were characterized and compared, first in terms of their nicotine self-administration behavior, then in terms of their nicotine/ethanol self-administration behavior, and lastly in terms of their self-administration of ethanol in the absence of nicotine. The results demonstrate that maternal consumption of fat compared to low-fat chow during gestation and lactation significantly stimulates nicotine self-administration during fixed-ratio testing. It also increases nicotine/ethanol self-administration during fixed-ratio and dose-response testing, with BEC elevated to 120 mg/dL, and causes an increase in breakpoint during progressive ratio testing. Of particular note is the finding that rats perinatally exposed to fat self-administer significantly more of the nicotine/ethanol mixture as compared to nicotine alone, an effect not evident in the chow-control rats. After removal of nicotine from the nicotine/ethanol mixture, this difference between the fat- and chow-exposed rats was lost, with both groups failing to acquire the self-administration of ethanol alone. Together, these findings suggest that perinatal exposure to a fat-rich diet, in addition to stimulating self-administration of nicotine, causes an even greater vulnerability to the excessive co-use of nicotine and ethanol.

---

**ABSTRACT**

The adverse effects of alcohol consumption during pregnancy are known, but the molecular events that lead to the phenotypic characteristics are unclear. To unravel the molecular mechanisms, we have used a mouse model of gestational ethanol exposure, which is based on maternal ad libitum ingestion of 10% (v/v) ethanol for the first 8 days of gestation (GD 0.5-8.5). Early neurulation takes place by the end of this period, which is equivalent to the developmental stage early in the fourth week post-fertilization in human. During this exposure period, dynamic epigenetic reprogramming takes place and the embryo is vulnerable to the effects of environmental factors. Thus, we hypothesize that early ethanol exposure disrupts the epigenetic reprogramming of the embryo, which leads to alterations in gene regulation and life-long changes in brain structure and function. Genome-wide analysis of gene expression in the mouse hippocampus revealed altered expression...
of 23 genes and three miRNAs in ethanol-exposed, adolescent offspring at postnatal day (P) 28. We confirmed this result by using two other tissues, where three candidate genes are known to express actively. Interestingly, we found a similar trend of upregulated gene expression in bone marrow and main olfactory epithelium. In addition, we observed altered DNA methylation in the CpG islands upstream of the candidate genes in the hippocampus. Our MRI study revealed asymmetry of brain structures in ethanol-exposed adult offspring (P60): we detected ethanol-induced enlargement of the left hippocampus and decreased volume of the left olfactory bulb. Our study indicates that ethanol exposure in early gestation can cause changes in DNA methylation, gene expression, and brain structure of offspring. Furthermore, the results support our hypothesis of early epigenetic origin of alcohol-induced disorders: changes in gene regulation may have already taken place in embryonic stem cells and therefore can be seen in different tissue types later in life.

Read Full Article
Back to Table of Contents

83. Paternal alcohol exposure in mice alters brain NGF and BDNF and increases ethanol-elicited preference in male offspring.


ABSTRACT
Ethanol (EtOH) exposure during pregnancy induces cognitive and physiological deficits in the offspring. However, the role of paternal alcohol exposure (PAE) on offspring EtOH sensitivity and neurotrophins has not received much attention. The present study examined whether PAE may disrupt nerve growth factor (NGF) and/or brain-derived neurotrophic factor (BDNF) and affect EtOH preference/rewarding properties in the male offspring. CD1 sire mice were chronically addicted for EtOH or administered with sucrose. Their male offsprings when adult were assessed for EtOH preference by a conditioned place preference paradigm. NGF and BDNF, their receptors (p75NTR, TrkA and TrkB), dopamine active transporter (DAT), dopamine receptors D1 and D2, pro-NGF and pro-BDNF were also evaluated in brain areas. PAE affected NGF levels in frontal cortex, striatum, olfactory lobes, hippocampus and hypothalamus. BDNF alterations in frontal cortex, striatum and olfactory lobes were found. PAE induced a higher susceptibility to the EtOH rewarding effects mostly evident at the lower concentration (0.5 g/kg) that was ineffective in non-PAE offspring. Moreover, higher ethanol concentrations (1.5 g/kg) produced an aversive response in PAE animals and a significant preference in non-PAE offspring. PAE affected also TrkA in the hippocampus and p75NTR in the frontal cortex. DAT was affected in the olfactory lobes in PAE animals treated with 0.5 g/kg of ethanol while no differences were found on D1/D2 receptors and for pro-NGF or pro-BDNF. In conclusion, this study shows that: PAE affects NGF and BDNF expression in the mouse brain; PAE may induce ethanol intake preference in the male offspring.

Read Full Article
Back to Table of Contents


84. Ethanol exposure induces neonatal neurodegeneration by enhancing CB1R Exon1 histone H4K8 acetylation and up-regulating CB1R function causing neurobehavioral abnormalities in adult mice.

Subbanna S, Nagre NN, Umapathy NS, Pace BS, Basavarajappa BS. (USA); Basavaraj@nki.rfmh.org

www.nofas-uk.org
ABSTRACT

BACKGROUND:

Ethanol exposure to rodents during postnatal day 7 (P7), which is comparable to the third trimester of human pregnancy, induces long-term potentiation and memory deficits. However, the molecular mechanisms underlying these deficits are still poorly understood.

METHODS:

In the present study, we explored the potential role of epigenetic changes at cannabinoid type 1 (CB1R) exon1 and additional CB1R functions, which could promote memory deficits in animal models of fetal alcohol spectrum disorder.

RESULTS:

We found that ethanol treatment of P7 mice enhances acetylation of H4 on lysine 8 (H4K8ace) at CB1R exon1, CB1R binding as well as the CB1R agonist-stimulated GTPγS binding in the hippocampus and neocortex, two brain regions that are vulnerable to ethanol at P7 and are important for memory formation and storage, respectively. We also found that ethanol inhibits cyclic adenosine monophosphate response element-binding protein (CREB) phosphorylation and activity-regulated cytoskeleton-associated protein (Arc) expression in neonatal and adult mice. The blockade or genetic deletion of CB1Rs prior to ethanol treatment at P7 rescued CREB phosphorylation and Arc expression. CB1R knockout mice exhibited neither ethanol-induced neurodegeneration nor inhibition of CREB phosphorylation or Arc expression. However, both neonatal and adult mice did exhibit enhanced CREB phosphorylation and Arc protein expression. P7 ethanol-treated adult mice exhibited impaired spatial and social recognition memory, which were prevented by the pharmacological blockade or deletion of CB1Rs at P7.

CONCLUSIONS:

Together, these findings suggest that P7 ethanol treatment induces CB1R expression through epigenetic modification of the CB1R gene, and that the enhanced CB1R function induces pCREB, Arc, spatial, and social memory deficits in adult mice.

Read Full Article
Back to Table of Contents


85. Prenatal ethanol exposure impairs executive function in mice into adulthood.

Marquardt K, Sigdel R, Caldwell K, Brigman JL. (USA)

ABSTRACT

BACKGROUND:

Despite evidence that prenatal alcohol exposure (PAE) can lead to a wide range of impairments in cognitive, social, and emotional behaviors, drinking during pregnancy remains common. Although there is a general understanding that high levels of drinking during pregnancy are unsafe, conflicting evidence regarding the impact of low intake may account for the persistence of this behavior.

METHODS:

To investigate the effects of PAE on learning and executive control, we utilized a voluntary paradigm where pregnant mice had access to a saccharin-sweetened 10% alcohol solution for 4 hours, during the dark cycle, throughout gestation. Male and female offspring were tested as adults on a touch-screen discrimination and reversal task mediated by corticostral circuits.

RESULTS:

Consistent with previous findings, PAE did not lead to gross morphological, motor, or sensory alterations in offspring. Both PAE and saccharin control female mice were slower to acquire the discrimination than males, but PAE did not impair associative learning in either sex. During reversal,
PAE led to a specific and significant impairment in the early phase, where cortical control is most required to flexibly alter choice behavior. PAE mice showed a significant increase in maladaptive perseverative responses but showed intact learning of the new association during late reversal.

CONCLUSIONS:
Previously, data from clinical studies have suggested that executive control deficits may underlie cognitive, as well as social, problems seen in adolescents with documented PAE. These data demonstrate that even more moderate alcohol exposure during development can lead to impaired cognitive functioning well into adulthood.

Read Full Article
Back to Table of Contents

Physiol Behav. 2015 Jan 7. pii: S0031-9384(15)00003-7. doi: 10.1016/j.physbeh.2015.01.001. [Epub ahead of print]

Popoola DO, Borrow AP, Sanders JE, Nizhnikov ME, Cameron NM. (USA); ncameron@binghamton.edu

ABSTRACT
Gestational alcohol use is well documented as detrimental to both maternal and fetal health, producing an increase in offspring’s tendency for alcoholism, as well as in behavioral and neuropsychological disorders. In both rodents and in humans, parental care can influence the development of offspring physiology and behavior. Animal studies that have investigated gestational alcohol use on parental care and/or their interaction mostly employ heavy alcohol use and single strains. This study aimed at investigating the effects of low gestational ethanol dose on parental behavior and its transgenerational transmission, with comparison between two rat strains. Pregnant Sprague Dawley (SD) and Long Evans (LE) progenitor dams (F0) received 1g/kg ethanol or water through gestational days 17–20 via gavage, or remained untreated in their home cages. At maturity, F1 female offspring were mated with males of the same strain and treatment and were left undisturbed through gestation. Maternal behavior was scored in both generations during the first six postnatal days. Arch-back nursing (ABN) was categorized as: 1, when the dam demonstrated minimal kyphosis; 2, when the dam demonstrated moderate kyphosis; and 3, when the dam displayed maximal kyphosis. Overall, SD showed greater amounts of ABN than LE dams and spent more time in contact with their pups. In the F0 generation, water and ethanol gavage increased ABN1 and contact with pups in SD, behaviors which decreased in treated LE. For ABN2, ethanol-treated SD dams showed more ABN2 than water-treated dams, with no effect of treatment on LE animals. In the F1 generation, prenatal exposure affected retrieval. Transgenerational transmission of LG was observed only in the untreated LE group. Strain-specific differences in maternal behavior were also observed. This study provides evidence that gestational gavage can influence maternal behavior in a strain-specific manner. Our results also suggest that the experimental procedure during gestation and genetic variations between strains may play an important role in the behavioral effects of prenatal manipulations.

Read Full Article
Back to Table of Contents

87. [Potential therapy of intravenous neural stem cell transplantation for psychiatric disorder—a strategy for facilitation of neural network and behavioral recovery].
www.nofas-uk.org
ABSTRACT
Recent clinical neuroimaging studies have revealed a possible relationship between morphological brain changes and the manifestation of psychiatric disorders such as depression, schizophrenia, and alcoholism. Although its biological mechanism is still unclear, the emerging evidence suggests that the alteration of neurogenesis is the key factor for the morphological brain changes of these psychiatric disorders. In our previous work, we analyzed the mechanism of neural network disruption by ethanol using cultured cells, and found a suppressive effect of ethanol on neural stem cell (NSC) differentiation. While, we also demonstrated that antidepressants, mood stabilizers and atypical antipsychotics stimulate NSC differentiation which was inhibited by ethanol. In the present work, we have demonstrated that the usefulness of intravenous transplantation of NSCs to fetal alcohol spectrum disorder (FASD) model rat for the purpose of reconstructing the impaired neural network and investigating the possibility of regenerative therapy for patients with neurobehavioral deficits of FASD. We have shown the potential migration of transplanted NSCs into the brain by visualizing a fluorescent cell marker and radioisotope, as well as the possible recovery of behavioral abnormalities observed in FASD model rats, such as memory/cognitive function, and social interaction. We further assessed the characteristics of transplanted cells in the brain and found that the GABAergic interneurons were increased in amygdala, DG, cingulated cortex areas in the model rat. In the amygdala and cingulate Cortex of model rats, number of parvalbumin positive cells was reduced and the NSC transplantation recovered these disturbances. Moreover, in the amygdala and cingulate cortex, intravenous NSC transplantation appears to regenerate expression of postsynaptic density protein 95 (PSD95) in FASD model rats. These results indicate that intravenous NSC transplantation has the potential to become a therapeutic intervention for FASD patients.

Read Full Article
Back to Table of Contents


88. Embryo transfers between C57BL/6J and DBA/2J mice: Examination of a maternal effect on ethanol teratogenesis.
Gilliam D. (USA)

ABSTRACT
Genetic factors influence fetal alcohol spectrum disorders (FASDs) in both humans and animals. Experiments using inbred and selectively bred mouse stocks that controlled for (1) ethanol dose, (2) maternal and fetal blood ethanol levels, and (3) fetal developmental exposure stage, show genotype can affect teratogenic outcome. Other experiments distinguish the teratogenic effects mediated by maternal genotype from those mediated by fetal genotype. One technique to distinguish maternal versus fetal genotype effect is to utilize embryo transfers. This study is the first to examine ethanol teratogenesis - fetal weight deficits and mortality, and digit, kidney, and vertebral malformations - in C57BL/6J (B6) and DBA/2J (D2) fetuses that were transferred as blastocysts into B6 and D2 dams. We hypothesized that, following maternal alcohol exposure, B6 and D2 fetuses gestating within B6 mothers, as compared to D2 mothers, will exhibit a higher frequency of malformations. On day 9 of pregnancy, females were intubated (IG) with either 5.8 g/kg ethanol (E) or maltose-dextrin (MD). Other females were mated within strain and treated with either ethanol or maltose, or were not exposed to either treatment. Implantation rates were affected by genotype. Results show more B6 embryos implanted into D2 females than B6 females (p < 0.05; 47% vs. 23%, respectively). There was no difference in the percentage of D2 embryos implanting into B6 and D2 females (14 and 16%, respectfully). Litter mortality averaged 24% across all experimental groups. Overall, in utero ethanol exposure reduced mean litter weight compared to maltose treatment (E = 1.01 g; MD = 1.19 g; p < 0.05); but maltose exposed litters with transferred embryos weighed more than similarly treated natural litters (1.30 g vs. 1.11 g; p < 0.05). Approximately 50% of all ethanol exposed B6 fetuses exhibited some malformation (digit, vertebral, and/or kidney)
Regardless of whether they were transferred into a B6 or D2 female, or were naturally conceived. This suggests the D2 maternal uterine environment did not offer any protection against ethanol teratogenesis for B6 fetuses. One of the questions remaining is the how the B6 uterine environment affects D2 teratogenesis. No definitive conclusions can be drawn because too few viable D2 litters were produced.

Read Full Article
Back to Table of Contents


89. CB1-receptor knockout neonatal mice are protected against ethanol-induced impairments of DNMT1, DNMT3A, and DNA methylation.
Nagre NN, Subbanna S, Shivakumar M, Psychoyos D, Basavarajappa BS. (USA)

ABSTRACT
The significant consequences of ethanol use during pregnancy are neurobehavioral abnormalities involving hippocampal and neocortex malfunctions that cause learning and memory deficits collectively named fetal alcohol spectrum disorder. However, the molecular mechanisms underlying these abnormalities are still poorly understood and therefore warrant systematic research. Here, we document novel epigenetic abnormalities in the mouse model of fetal alcohol spectrum disorder. Ethanol treatment of P7 mice, which induces activation of caspase 3, impaired DNA methylation through reduced DNA methyltransferases (DNMT1 and DNMT3A) levels. Inhibition of caspase 3 activity, before ethanol treatment, rescued DNMT1, DNMT3A proteins as well as DNA methylation levels. Blockade of histone methyltransferase (G9a) activity or cannabinoid receptor type-1 (CB1R), prior to ethanol treatment, which, respectively, inhibits or prevents activation of caspase 3, rescued the DNMT1 and DNMT3A proteins and DNA methylation. No reduction of DNMT1 and DNMT3A proteins and DNA methylation was found in P7 CB1R null mice, which exhibit no ethanol-induced activation of caspase 3. Together, these data demonstrate that ethanol-induced activation of caspase 3 impairs DNA methylation through DNMT1 and DNMT3A in the neonatal mouse brain, and such impairments are absent in CB1R null mice. Epigenetic events mediated by DNA methylation may be one of the essential mechanisms of ethanol teratogenesis. Schematic mechanism of action by which ethanol impairs DNA methylation. Studies have demonstrated that ethanol has the capacity to bring epigenetic changes to contribute to the development of fetal alcohol spectrum disorder (FASD). However, the mechanisms are not well studied. P7 ethanol induces the activation of caspase 3 and impairs DNA methylation through reduced DNA methyltransferases (DNMT1 and DNMT3A) proteins (→). The inhibition or genetic ablation of cannabinoid receptor type-1 or inhibition of histone methyltransferase (G9a) by Bix (-----) or inhibition of caspase 3 activation by Q-quinoline-Val-Asp(Ome)-CH2-O-phenoxy (Q-VD-OPh) (↓) rescue loss of DNMT1, DNMT3A as well as DNA methylation. Hence, the putative DNMT1/DNMT3A/DNA methylation mechanism may have a potential regulatory role in FASD.

Read Full Article
Back to Table of Contents


90. Fetal alcohol exposure increases susceptibility to carcinogenesis and promotes tumor progression in prostate gland.
Sarkar DK. (USA); sarkar@aesop.rutgers.edu

www.nofas-uk.org
ABSTRACT
The idea that exposure to adverse environmental conditions and lifestyle choices during pregnancy can result in fetal programming that underlies disease susceptibility in adulthood is now widely accepted. Fetal alcohol exposed offspring displays many behavioral and physiological abnormalities including neuroendocrine-immune functions, which often carry over into their adult life. Since the neuroendocrine-immune system plays an important role in controlling tumor surveillance, fetal alcohol exposed offspring can be vulnerable to develop cancer. Animal studies have recently showed increased cancer growth and progression in various tissues of fetal alcohol exposed offspring. I will detail in this chapter the recent evidence for increased prostate carcinogenesis in fetal alcohol exposed rats. I will also provide evidence for a role of excessive estrogenization during prostatic development in the increased incidence of prostatic carcinoma in these animals. Furthermore, I will discuss the additional possibility of the involvement of impaired stress regulation and resulting immune incompetence in the increased prostatic neoplasia in the fetal alcohol exposed offspring.

Read Full Article
Back to Table of Contents

91. Choline partially prevents the impact of ethanol on the lipid raft dependent functions of L1 cell adhesion molecule.
Tang N, Bamford P, Jones J, He M, Kane MA, Mooney SM, Bearer CF. (USA)

ABSTRACT
BACKGROUND:
Fetal alcohol spectrum disorder, the leading known cause of mental retardation, is caused by alcohol exposure during pregnancy. One mechanism of ethanol (EtOH) teratogenicity is the disruption of the functions of L1 cell adhesion molecule (L1). These functions include enhancement of neurite outgrowth, trafficking through lipid rafts, and signal transduction. Recent data have shown that choline supplementation of rat pups reduces the effects of EtOH on neurobehavior. We sought to determine whether choline could prevent the effect of EtOH on L1 function using a simple experimental system.

METHODS:
Cerebellar granule neurons (CGN) from postnatal day 6 rat pups were cultured with and without supplemental choline, and the effects on L1 signaling, lipid raft distribution, and neurite outgrowth were measured in the presence or absence of EtOH.

RESULTS:
Choline significantly reduced the effect of EtOH on L1 signaling, the distribution of L1 in lipid rafts and L1-mediated neurite outgrowth. However, choline supplemented EtOH-exposed cultures remained significantly different than controls.

CONCLUSIONS:
Choline pretreatment of CGN significantly reduces the disruption of L1 function by EtOH, but does not completely return L1 function to baseline. This experimental system will enable discovery of the mechanism of the neuroprotective effect of choline.

Read Full Article
Back to Table of Contents
92. Zinc insufficiency mediates ethanol-induced alveolar macrophage dysfunction in the pregnant female mouse.
Konomi JV, Harris FL, Ping XD, Gauthier TW, Brown LA. (USA); lbrow03@emory.edu

ABSTRACT

AIMS:
(a) Establish the minimum number of weeks of chronic ethanol ingestion needed to perturb zinc homeostasis, (b) Examine intracellular zinc status in the alveolar macrophages (AMs) when ethanol ingestion is combined with pregnancy, (c) Investigate whether in vitro zinc treatment reverses the effects of ethanol ingestion on the AM.

METHODS:
C57BL/6 female mice were fed a liquid diet (±25% ethanol-derived calories) during preconception and pregnancy. The control group was pair-fed to the ethanol group. In the isolated AMs, we measured intracellular AM zinc levels, zinc transporter expression, alternative activation and phagocytic index. Zinc acetate was added to some cells prior to analysis.

RESULTS:
Intracellular zinc levels in the AM decreased within 3 weeks of ethanol ingestion. After ethanol ingestion prior to and during pregnancy, zinc transporter expression and intracellular zinc levels were decreased in the AMs when compared with controls. Bacterial clearance was decreased because the AMs were alternatively activated. In vitro additions of zinc reversed these effects of ethanol.

CONCLUSION:
Ethanol ingestion prior to and during pregnancy perturbed AM zinc balance resulting in impaired bacterial clearance, but these effects were ameliorated by in vitro zinc treatments.

Read Full Article
Back to Table of Contents

Neuropsychol Rev. 2015 Jun 3. [Epub ahead of print]

93. Executive Functioning in Children and Adolescents Prenatally Exposed to Alcohol: A Meta-Analytic Review.
Khoury JE, Milligan K, Girard TA. (Canada); jennifer.khoury@psych.ryerson.ca

ABSTRACT

Prenatal alcohol exposure is associated with a constellation of adverse physical, neurocognitive and behavior outcomes, which comprise a continuum of disorders labeled Fetal Alcohol Spectrum Disorders (FASD). Extant research has consistently identified executive functions (EF) as a central impairment associated with FASD. Despite this, heterogeneity exists regarding the strength of the association between FASD and different EF, and this association has not yet been quantitatively synthesized. The current meta-analysis reviews 46 studies that compare children and adolescents with FASD to participants without FASD, on a variety of EF measures. In accordance with Miyake et al. Cognitive Psychology, 41, 49-100 (2000) three-factor model of EF, findings for the primary EF domains of working memory, inhibition, and set shifting are reviewed. Results indicate that children and adolescents with FASD demonstrate significant deficits across these EF, although the magnitude of effects diverged between EF, with working memory and inhibition yielding medium effects and set shifting yielding large effects. These results were moderated by sample characteristics, type of FASD diagnosis, and EF methodology. This quantitative synthesis offers novel future research directions.
94. Anterior Cingulate Cortex Surface Area Relates to Behavioral Inhibition in Adolescents with and without Heavy Prenatal Alcohol Exposure.
Migliorini R, Moore EM, Glass L, Infante MA, Tapert SF, Jones KL, Mattson SN, Riley EP. (USA); ramiglio@ucsd.edu

ABSTRACT
Prenatal alcohol exposure is associated with behavioral disinhibition, yet the brain structure correlates of this deficit have not been determined with sufficient detail. We examined the hypothesis that the structure of the anterior cingulate cortex (ACC) relates to inhibition performance in youth with histories of heavy prenatal alcohol exposure (AE, n=32) and non-exposed controls (CON, n=21). Adolescents (12-17y) underwent structural magnetic resonance imaging yielding measures of gray matter volume, surface area, and thickness across four ACC subregions. A subset of subjects were administered the NEPSY-II Inhibition subtest. MANCOVA was utilized to test for group differences in ACC and inhibition performance and multiple linear regression was used to probe ACC-inhibition relationships. ACC surface area was significantly smaller in AE, though this effect was primarily driven by reduced right caudal ACC (rcACC). AE also performed significantly worse on inhibition speed but not on inhibition accuracy. Regression analyses with the rcACC revealed a significant group x ACC interaction. A smaller rcACC surface area was associated with slower inhibition completion time for AE but was not significantly associated with inhibition in CON. After accounting for processing speed, smaller rcACC surface area was associated with worse (i.e., slower) inhibition regardless of group. Examining processing speed independently, decrease in rcACC surface area was associated with faster processing speed for CON but not significantly associated with processing speed in AE. Results support the theory that caudal ACC may monitor reaction time in addition to inhibition and highlight the possibility of delayed ACC neurodevelopment in prenatal alcohol exposure.

95. MiR-125b protects against ethanol-induced apoptosis in neural crest cells and mouse embryos by targeting Bak1 and PUMA.
Chen X, Liu J, Feng WK, Wu X, Chen SY. (USA); shaoyu.chen@louisville.edu

ABSTRACT
MicroRNAs are a class of small noncoding RNAs that have been implicated in regulation of a broad range of cellular and physiologic processes, including apoptosis. The objective of this study is to elucidate the roles of miR-125b in modulating ethanol-induced apoptosis in neural crest cells (NCCs) and mouse embryos. We found that treatment with ethanol resulted in a significant decrease in miR-125b expression in NCCs and in mouse embryos. We also validated that Bcl-2 antagonist killer 1 (Bak1) and p53-upregulated modulator of apoptosis (PUMA) are the direct targets of miR-125b in NCCs. In addition, over-expression of miR-125b significantly reduced ethanol-induced increase in Bak1 and PUMA protein expression, caspase-3 activation, and apoptosis in NCCs, indicating that miR-125b can modulate ethanol-induced apoptosis by the regulation of Bcl-2 and p53 pathways. Furthermore, microinjection of miR-125b mimic resulted in a significant increase in miR-125b expression and a decrease in the protein expression of Bak1 and PUMA in ethanol-exposed mouse embryos. Up-regulation of miR-125b also significantly reduced ethanol-induced caspase-3 activation and diminished ethanol-induced growth retardation in mouse embryos. This is the first
demonstration that miR-125b can prevent ethanol-induced apoptosis and that microinjection of miRNA mimic can prevent ethanol-induced embryotoxicity.

Read Full Article

Back to Table of Contents

96. Preventing alcohol-exposed pregnancy among an American Indian/Alaska Native population: effect of a screening, brief intervention, and referral to treatment intervention.
Montag AC, Brodine SK, Alcaraz JE, Clapp JD, Allison MA, Calac DJ, Hull AD, Gorman JR, Jones KL, Chambers CD. (USA)

ABSTRACT

BACKGROUND:
Fetal alcohol spectrum disorders are the result of alcohol-exposed pregnancies (AEP) and believed to be the leading known cause of developmental disabilities in the United States. Our objective was to determine whether a culturally targeted Screening, Brief Intervention, and Referral to Treatment (SBIRT) intervention may reduce risky drinking and vulnerability to AEP among American Indian/Alaska Native (AIAN) women in Southern California.

METHODS:
Southern California AIAN women of childbearing age who completed a survey including questions regarding alcohol consumption and contraceptive use were randomized into intervention or treatment as usual groups where the former group completed an online SBIRT intervention, and were followed up at 1, 3, and 6 months postintervention.

RESULTS:
Of 263 women recruited and 247 with follow-up data, one-third were at high risk of having an AEP at baseline. Both treatment groups decreased self-reported risky drinking behavior (drinks per week, \( p < 0.001 \); frequency of heavy episodic [binge] drinking episodes per 2 weeks, \( p = 0.017 \) and risk of AEP \( p < 0.001 \) at 6 months postintervention) in the follow-up period. There was no difference between treatment groups. Baseline factors associated with decreased risk of an AEP at follow-up included the perception that other women in their peer group consumed a greater number of drinks per week, having reported a greater number of binge episodes in the past 2 weeks, and depression/impaired functionality.

CONCLUSIONS:
Participation in assessment alone may have been sufficient to encourage behavioral change even without the web-based SBIRT intervention. Randomization to the SBIRT did not result in a significantly different change in risky drinking behaviors. The importance of perception of other women's drinking and one's own depression/functionality may have implications for future interventions.

Read Full Article

Back to Table of Contents


97. Ethanol deregulates Mecp2/MeCP2 in differentiating neural stem cells via interplay between 5-methylcytosine and 5-hydroxymethylcytosine at the Mecp2 regulatory elements.
Liyanage VR, Zachariah RM, Davie JR, Rastegar M. (Canada); umbatuwi@myumanitoba.ca, mojgan.rastegar@umanitoba.ca
ABSTRACT
Methyl CpG Binding Protein 2 (MeCP2) is an important epigenetic factor in the brain. MeCP2 expression is affected by different environmental insults including alcohol exposure. Accumulating evidence supports the role of aberrant MeCP2 expression in ethanol exposure-induced neurological symptoms. However, the underlying molecular mechanisms of ethanol-induced MeCP2 deregulation remain elusive. To study the effect of ethanol on Mecp2/MeCP2 expression during neurodifferentiation, we established an in vitro model of ethanol exposure, using differentiating embryonic brain-derived neural stem cells (NSC). Previously, we demonstrated the impact of DNA methylation at the Mecp2 regulatory elements (REs) on Mecp2/MeCP2 expression in vitro and in vivo. Here, we studied whether altered DNA methylation at these REs is associated with the Mecp2/MeCP2 misexpression induced by ethanol. Binge-like and continuous ethanol exposure upregulated Mecp2/MeCP2, while ethanol withdrawal downregulated its expression. DNA methylation analysis by methylated DNA immunoprecipitation indicated that increased 5-hydroxymethylcytosine (5hmC) and decreased 5-methylcytosine (5mC) enrichment at specific REs were associated with upregulated Mecp2/MeCP2 following continuous ethanol exposure. The reduced Mecp2/MeCP2 expression upon ethanol withdrawal was associated with reduced 5hmC and increased 5mC enrichment at these REs. Moreover, ethanol altered global DNA methylation (5mC and 5hmC). Under the tested conditions, ethanol had minimal effects on NSC cell fate commitment, but caused changes in neuronal morphology and glial cell size. Taken together, our data represent an epigenetic mechanism for ethanol-mediated misexpression of Mecp2/MeCP2 in differentiating embryonic brain cells. We also show the potential role of DNA methylation and MeCP2 in alcohol-related neurological disorders, specifically Fetal Alcohol Spectrum Disorders.

Read Full Article
Back to Table of Contents

98. Ethanol exposure induces a delay in the reacquisition of function during head regeneration in Schmidtea mediterranea.
Lowe JR, Mahool TD, Staehle MM. (USA); lowej777@gmail.com, tyler.mahool@gmail.com, staehle@rowan.edu

ABSTRACT
Prenatal exposure to ethanol affects neurodevelopmental processes, leading to a variety of physical and cognitive impairments collectively termed Fetal Alcohol Spectrum Disorders (FASD). The molecular level ethanol-induced alterations that underlie FASD are poorly understood and are difficult to study in mammals. Ethanol exposure has been shown to affect regulation and differentiation of embryonic stem cells in vitro, suggesting that in vivo effects such as FASD could arise from similar alterations of stem cells. In this study, we hypothesize that ethanol exposure affects head regeneration and neuroregeneration in the Schmidtea mediterranea planarian. S. mediterranea freshwater flatworms have remarkable regenerative abilities arising from an abundant population of pluripotent adult somatic stem cells known as neoblasts. Here, we evaluated the mobility-normalized photophobic behavior of ethanol-exposed planaria as an indicator of cognitive function in intact and head-regenerating worms. Our studies show that exposure to 1% ethanol induces a delay in the reacquisition of behavior during head regeneration that cannot be attributed to the effect of ethanol on intact worms. This suggests that the S. mediterranea planarian could provide insight into conserved neurodevelopmental processes that are affected by ethanol and that lead to FASD in humans.

Read Full Article
Back to Table of Contents
99. Experimental Models of Early Exposure to Alcohol: A Way to Unravel the Neurobiology of Mental Retardation
Alberto Granato, Andrea De Giorgio, (Italy), otrobliatanarg@ttaciniu.it

ABSTRACT
As of November 2014, a PubMed search for “fetal alcohol” retrieved more than 14,500 articles. Alcohol consumption during pregnancy and its detrimental consequences on the developing brain raise major public health, social, and economic issues. However, the research on fetal alcohol spectrum disorders (FASD) in the real world is challenging, given that it is largely based on retrospective analysis. Therefore, establishing the relationship between brain damage and drinking habits proves particularly hard. One of the advantages of FASD studies carried out in the laboratory environment derives from the tight control of time, dose, and modality of alcohol exposure (1). Furthermore, since FASD are among the leading causes of intellectual disability, animal models of early exposure to alcohol represent an invaluable tool to elucidate the basic neurobiological mechanisms leading to the cognitive defects. Experimental models of genetic syndromes are ideally suited to study the role of single molecules, such as the fragile X mental retardation protein, throughout the maturation of the nervous system. Conversely, experimental exposure to alcohol can be carried out during discrete, often very restricted, time windows and, though depending on the interference with several molecular pathways, can provide information about which developmental periods and brain areas are critically involved in the genesis of the intellectual disability.

In the present Research Topic, hosted by Frontiers in Pediatrics, we have gathered some of the most outstanding scientists, among those actively involved in the experimental study of FASD. The reader will be browsing through different subfields of basic research on FASD and we are confident that he/she will get a comprehensive view of the topic, including open questions and useful hints for novel therapeutic interventions.

Read Full Article
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4285074/
Back to Table of Contents

100. Community translation of the Math Interactive Learning Experience Program for children with FASD.
Kable JA, Taddeo E, Strickland D, Coles CD. (USA), jkabl01@emory.edu

ABSTRACT
The Math Interactive Learning Experience (MILE), a program designed to address academic and behavioral problems found in children with Fetal Alcohol Spectrum Disorders (FASD), was found to be effective in a randomized clinical trials with results that persisted at a 6-month follow-up. The current study evaluated the effectiveness of a community translation, in partnership with several community sites in the metropolitan Atlanta area. A total of 60 participants were randomly assigned to one of the three treatment groups: the MILE program administered at a specialty care center (Center MILE) or in the community (Community MILE), or to parent math instruction only (Parent Instruction). This study evaluated instructor satisfaction with the training program, knowledge related to FASD and the MILE program, adherence to the MILE teaching methodology, participant math outcomes, and parents' satisfaction with their treatment experience. Instructors reported a high degree of satisfaction with the overall training and mean site fidelity ratings were positively correlated with change in math performance. Those in the MILE intervention groups demonstrated more positive gains in math skills than those in the Parent Instruction group but did not differ from each other. Parents in the Parent Instruction group reported less satisfaction with their intervention than those assigned to the Center MILE group but satisfaction ratings did not differ between those in the MILE intervention groups. These results indicate that the community translation and the MILE instructor training program developed as part of this process were well-received and effective in producing positive treatment outcomes.
101. **Misdiagnosis and missed diagnoses in foster and adopted children with prenatal alcohol exposure.**
Chasnoff IJ, Wells AM, King L. (USA), ichasnoff@cr-triangle.org

**ABSTRACT**

**OBJECTIVE:**
The purpose of this article is to assess the rate of misdiagnosis and missed diagnoses of fetal alcohol spectrum disorders (FASD) among a population of foster and adopted youth referred to a children's mental health center.

**METHODS:**
Data were collected from a sample of 547 children who underwent a comprehensive multidisciplinary diagnostic evaluation. Utilizing current diagnostic criteria, children were diagnosed, as appropriate, with fetal alcohol syndrome, partial fetal alcohol syndrome, alcohol-related neurodevelopmental disorder, or alcohol-related birth defects. Changes in rates of alcohol exposure-related diagnoses and cooccurring mental health disorders pre- and postassessment were analyzed by using McNemar's test for dependent proportions.

**RESULTS:**
Among 156 children and adolescents who met criteria for a diagnosis within the fetal alcohol spectrum, 125 had never been diagnosed as affected by prenatal alcohol exposure, a missed diagnosis rate of 80.1%. Of the 31 who had been recognized before referral as affected by prenatal alcohol exposure, 10 children's FASD diagnoses were changed within the spectrum, representing a misdiagnosis rate of 6.4%. The remaining 21 (13.5%) children's diagnoses stayed the same. There also were significant changes in the rate of mental health diagnosis, and learning disorders, communication disorders, and intellectual disability, objective signs of neurocognitive damage, were not recognized in a significant number of children with FASD.

**CONCLUSIONS:**
Within this clinical sample, 86.5% of youth with FASD had never been previously diagnosed or had been misdiagnosed. These high rates of missed diagnoses and misdiagnosis have significant implications for intervention and therapeutic services.

Read Full Article

102. **Salivary cortisol levels are elevated in the afternoon and at bedtime in children with prenatal alcohol exposure.**
Keiver K, Bertram CP, Orr AP, Clarren S. (Canada), kathy.keiver@ufv.ca

**ABSTRACT**
Prenatal alcohol exposure can cause dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, which may underlie some of the behavioral and adaptive problems seen in individuals with Fetal Alcohol Spectrum Disorders (FASD). Infants prenatally exposed to alcohol show altered basal and post-stress cortisol levels, but it is unknown if this persists beyond 2 years of age. It is also unknown if cortisol levels can be normalized through intervention programs. In this study, we investigated the effects of a physical activity program for children with FASD to determine: 1) if HPA dysregulation
persists in school-age children with FASD, and 2) the effect of our program on cortisol levels. Twenty six children (ages 6-14 years) with FASD participated in an 8 week motor skill development program. Salivary cortisol levels were measured in 24 children and compared at 4 time points: before, immediately after, 3 months, and 1 year after program completion. Cortisol levels were also compared to 32 control children to evaluate the long-term effects of prenatal alcohol exposure on HPA regulation. For each time point, saliva was collected on each of 2 days at 3 times in the diurnal cycle: awakening, after school, and just before bedtime. Cortisol levels were significantly higher in the afternoon and at bedtime in children with FASD with confirmed prenatal exposure to high levels of alcohol (alcohol exposure rank 4), compared with Control children or children with FASD with exposure to low or unknown levels of alcohol (alcohol exposure rank 3). The program did not significantly affect cortisol levels in children with FASD as a group. These results provide support for long-term effects of prenatal alcohol exposure on the HPA system in humans, which could increase vulnerability to mental health issues and diseases later in life.

Read Full Article
Back to Table of Contents

103. Epigenetics in pediatrics.
Puumala SE, Hoyme HE. (USA)

ABSTRACT
Epigenetic mechanisms are external modifications of DNA that cause changes in gene function and are involved in many diseases. Specific examples of pediatric diseases with a known or suspected epigenetic component include Beckwith-Wiedemann syndrome, childhood leukemia, allergies, asthma, fetal alcohol spectrum disorders, childhood obesity, and type 2 diabetes mellitus. Currently, epigenetically active treatments are being used to treat childhood leukemia. Potential epigenetically active treatments and preventive regimens are under study for other diseases. Pediatricians need to be aware of the epigenetic basis of disease to help inform clinical decision making in the future.

Read Full Article
Back to Table of Contents

104. Embryonic alcohol exposure impairs the dopaminergic system and social behavioral responses in adult zebrafish.
Fernandes Y, Rampersad M, Gerlai R. (Canada), robertGerlai@yahoo.com

ABSTRACT
BACKGROUND:
The zebrafish is a powerful neurobehavioral genetics tool with which complex human brain disorders including alcohol abuse and fetal alcohol spectrum disorders may be modeled and investigated. Zebrafish innately form social groups called shoals. Previously, it has been demonstrated that a single bath exposure (24 hours postfertilization) to low doses of alcohol (0, 0.25, 0.50, 0.75, and 1% vol/vol) for a short duration (2 hours) leads to impaired group forming, or shoaling, in adult zebrafish.

METHODS:
In the current study, we immersed zebrafish eggs in a low concentration of alcohol (0.5% or 1% vol/vol) for 2 hours at 24 hours postfertilization and let the fish grow and reach adulthood. In addition
to quantifying the behavioral response of the adult fish to an animated shoal, we also measured the amount of dopamine and its metabolite 3,4-dihydroxyphenylacetic acid from whole brain extracts of these fish using high-pressure liquid chromatograph.

RESULTS:

Here we confirm that embryonic alcohol exposure makes adult zebrafish increase their distance from the shoal stimulus in a dose-dependent manner. We also show that the shoal stimulus increases the amount of dopamine and 3,4-dihydroxyphenylacetic acid in the brain of control zebrafish but not in fish previously exposed to alcohol during their embryonic development.

CONCLUSIONS:

We speculate that one of the mechanisms that may explain the embryonic alcohol-induced impaired shoaling response in zebrafish is dysfunction of reward mechanisms subserved by the dopaminergic system.

Read Full Article
Back to Table of Contents


105. Moderate prenatal alcohol exposure and quantification of social behavior in adult rats.
Hamilton DA, Magcalas CM, Barto D, Bird CW, Rodriguez CI, Fink BC, Pellis SM, Davies S, Savage DD. (USA), dahamilt@unm.edu

ABSTRACT

Alterations in social behavior are among the major negative consequences observed in children with Fetal Alcohol Spectrum Disorders (FASDs). Several independent laboratories have demonstrated robust alterations in the social behavior of rodents exposed to alcohol during brain development across a wide range of exposure durations, timing, doses, and ages at the time of behavioral quantification. Prior work from this laboratory has identified reliable alterations in specific forms of social interaction following moderate prenatal alcohol exposure (PAE) in the rat that persist well into adulthood, including increased wrestling and decreased investigation. These behavioral alterations have been useful in identifying neural circuits altered by moderate PAE(1), and may hold importance for progressing toward a more complete understanding of the neural bases of PAE-related alterations in social behavior. This paper describes procedures for performing moderate PAE in which rat dams voluntarily consume ethanol or saccharin (control) throughout gestation, and measurement of social behaviors in adult offspring.

Read Full Article
Back to Table of Contents


106. Psychosocial outcomes of fetal alcohol syndrome in adulthood.
Rangmar J, Hjern A, Vinnerljung B, Strömland K, Aronson M, Fahlke C. (Sweden), jenny.rangmar@psy.gu.se

ABSTRACT

BACKGROUND AND OBJECTIVE:

Primary disabilities in children prenatally exposed to alcohol have a major impact on their daily life. It is suggested that these issues persist into adulthood, but few studies have addressed the outcome in adults with prenatal exposure, especially those with fetal alcohol syndrome (FAS). The aim of this
A follow-up study was to investigate outcome variables, such as education, employment, health, and criminal acts, in 79 adults diagnosed with FAS.

METHODS:
We carried out a national register-based study of 79 adults with an FAS diagnosis, at a mean age of 32. Education, social adjustment, and mental health outcomes were analyzed and compared with 3160 comparison individuals matched on age, gender, and place of birth.

RESULTS:
The FAS group was much more likely to have received special education (25% vs 2%), be unemployed (51% vs 15%), and receive a disability pension (31% vs 3%) than the comparisons, but the levels of criminal offenses were similar. The FAS group had higher hospital admission rates for alcohol abuse (9% vs 2%) and psychiatric disorders (33% vs 5%) and was more likely to be prescribed psychotropic drugs (57% vs 27%).

CONCLUSIONS:
Swedish children with FAS have quite diverse psychosocial outcomes in adulthood, considerably worse than for majority population peers. Potential risk and protective factors within the FAS group deserve study to enable development of effective interventions.

Read Full Article
Back to Table of Contents

107. Comparisons of Intelligence and Behavior in Children With Fetal Alcohol Spectrum Disorder and ADHD.
Raldiris TL, Bowers TG, Towsey C. (USA), dvo@psu.edu

ABSTRACT
OBJECTIVE:
Children with fetal alcohol spectrum disorder (FASD) can easily be misdiagnosed as having ADHD.

METHOD:
A total of 164 children were compared on cognitive and behavioral measures for four groups of children: FASD, ADHD, FASD + ADHD, and other neuropsychological disorders.

RESULTS:
The ADHD group was not significantly different from the "other diagnosis" group on any of the measurements. The children with FASD were found to perform significantly worse than ADHD on externalizing problems, Full-Scale IQ, and indices of Verbal Comprehension, Perceptual Reasoning, and Working Memory. The comorbid FASD + ADHD group was significantly weaker than ADHD on verbal comprehension measures. The FASD children demonstrated significantly higher levels of atypicality and aggression relative to ADHD, and the FASD + ADHD group demonstrated significantly higher levels of hyperactivity and withdrawal relative to ADHD.

CONCLUSION:
These results indicate that children with FASD display a differential behavioral and cognitive profile that is significantly poorer than children with ADHD and other types of neuropsychological disorders.

Read Full Article
Back to Table of Contents
The effects of prenatal exposure to alcohol and environmental tobacco smoke on risk for ADHD: a large population-based study.
Han JY, Kwon HJ, Ha M, Paik KC, Lim MH, Gyu Lee S, Yoo SJ, Kim EJ. (South Korea), hojangkwon@gmail.com

ABSTRACT
Attention deficit hyperactivity disorder (ADHD) is caused by the interaction of genetic and environmental factors. The objective of this study was to examine the effects of prenatal exposure to alcohol and environmental tobacco smoke (ETS). Among the 30,552 parents who responded to a survey, the answers of 19,940 who replied to questions on prenatal exposure to ETS, alcohol consumption, and completed the DuPaul Rating Scale were analyzed. Results revealed that risk of ADHD significantly increased as a result of exposure to alcohol by 1.55 times (95% CI 1.33-1.82), maternal smoking during pregnancy by 2.64 times (95% CI 1.45-4.80), and paternal smoking during pregnancy by 1.17 times (95% CI 1.98-1.39). When the subjects whose mothers did not smoke during pregnancy were divided into 4 groups, the prevalence was 1.16 times higher (95% CI 1.02-1.33) in the group exposed to ETS but not alcohol, 1.19 times higher (95% CI 0.91-1.57) in the group exposed to alcohol but not ETS, and 1.58 times higher (95% CI 1.31-1.91) in the group exposed to ETS and alcohol. The differences between the groups were statistically significantly (P<0.0001). This result shows that simultaneous exposure to ETS and alcohol during pregnancy increases the risk of ADHD.

Read Full Article

Back to Table of Contents

A deficit in face-voice integration in developing vervet monkeys exposed to ethanol during gestation.
Zangenehpour S, Javadi P, Ervin FR, Palmour RM, Ptito M. (Canada, Denmark)

ABSTRACT
Children with fetal alcohol spectrum disorders display behavioural and intellectual impairments that strongly implicate dysfunction within the frontal cortex. Deficits in social behaviour and cognition are amongst the most pervasive outcomes of prenatal ethanol exposure. Our naturalistic vervet monkey model of fetal alcohol exposure (FAE) provides an unparalleled opportunity to study the neurobehavioral outcomes of prenatal ethanol exposure in a controlled experimental setting. Recent work has revealed a significant reduction of the neuronal population in the frontal lobes of these monkeys. We used an intersensory matching procedure to investigate audiovisual perception of socially relevant stimuli in young FAE vervet monkeys. Here we show a domain-specific deficit in audiovisual integration of socially relevant stimuli. When FAE monkeys were shown a pair of side-by-side videos of a monkey concurrently presenting two different calls along with a single audio track matching the content of one of the calls, they were not able to match the correct video to the single audio track. This was manifest by their average looking time being equally spent towards both the matching and non-matching videos. However, a group of normally developing monkeys exhibited a significant preference for the non-matching video. This inability to integrate and thereby discriminate audiovisual stimuli was confined to the integration of faces and voices as revealed by the monkeys' ability to match a dynamic face to a complex tone or a black-and-white checkerboard to a pure tone, presumably based on duration and/onset-offset synchrony. Together, these results suggest that prenatal ethanol exposure negatively affects a specific domain of audiovisual integration. This deficit is confined to the integration of information that is presented by the face and the voice and does not affect more elemental aspects of sensory integration.

Read Full Article

Back to Table of Contents
110. Maternal risk factors for fetal alcohol spectrum disorders in a province in Italy.

Mauro.Ceccanti@uniroma1.it, philip_may@unc.edu

ABSTRACT

BACKGROUND:
Maternal risk factors for fetal alcohol spectrum disorders (FASD) in Italy and Mediterranean cultures need clarification, as there are few studies and most are plagued by inaccurate reporting of antenatal alcohol use.

METHODS:
Maternal interviews (n = 905) were carried out in a population-based study of the prevalence and characteristics of FASD in the Lazio region of Italy which provided data for multivariate case control comparisons and multiple correlation models.

RESULTS:
Case control findings from interviews seven years post-partum indicate that mothers of children with FASD are significantly more likely than randomly-selected controls or community mothers to: be shorter; have higher body mass indexes (BMI); be married to a man with legal problems; report more drinking three months pre-pregnancy; engage in more current drinking and drinking alone; and have alcohol problems in her family. Logistic regression analysis of multiple candidate predictors of a FASD diagnosis indicates that alcohol problems in the child's family is the most significant risk factor, making a diagnosis within the continuum of FASD 9 times more likely (95%C.I. = 1.6 to 50.7). Sequential multiple regression analysis of the child's neuropsychological performance also identifies alcohol problems in the child's family as the only significant maternal risk variable (p < .001) when controlling for other potential risk factors.

CONCLUSIONS:
Underreporting of prenatal alcohol use has been demonstrated among Italian and other Mediterranean antenatal samples, and it was suspected in this sample. Nevertheless, several significant maternal risk factors for FASD have been identified.

Read Full Article

Back to Table of Contents

111. Effect of repeated alcohol exposure during the third trimester-equivalent on messenger RNA levels for interleukin-1β, chemokine (C-C motif) ligand 2, and interleukin 10 in the developing rat brain after injection of lipopolysaccharide.
Topper LA, Valenzuela CF. (USA); fvalenzuela@salud.unm.edu

ABSTRACT
Microglia undergo maturation during the third trimester of human development (equivalent to the first 1-2 weeks of postnatal life in rodents), during which these cells may be particularly sensitive to insult. Alcohol exposure during this period can activate the neuroimmune system, an effect that may contribute to the pathophysiology of fetal alcohol spectrum disorders. Here, we investigated whether repeated alcohol exposure during the third trimester-equivalent in rats has a priming effect on the neuroimmune response to injection of bacterial lipopolysaccharide (LPS). Pups were exposed to alcohol in vapor chambers for 4 h daily from postnatal day (PD)2 to PD16 (peak blood alcohol concentrations ~150 mg/dL). On PD17, rats were injected with either saline or LPS (50 μg/kg) and
the frontal cortex, cerebellar vermis, and dentate gyrus were collected 2 h later. Messenger RNA (mRNA) levels for the pro-inflammatory agents interleukin 1β (IL-1β) and chemokine (C-C) motif ligand 2 (CCL2), as well as levels of the anti-inflammatory cytokine interleukin 10 (IL-10), were measured using reverse transcriptase polymerase chain reaction. LPS consistently increased IL-1β and CCL2 mRNA levels in the dentate gyrus, frontal cortex, and cerebellum of both male and female rats. Furthermore, the LPS-induced increase of IL-1β mRNA levels was significantly blunted in the frontal cortex of alcohol-exposed female rats. Conversely, LPS only minimally affected IL-10 mRNA expression and there were no significant differences between air- and alcohol-exposed rats. Taken together with the literature regarding the effect of third-trimester alcohol exposure on the neuroimmune system, our findings suggest that chronic exposure to lower levels is less disruptive to the neuroimmune system than binge-like exposure to high doses of alcohol.

Read Full Article

Cerebellum. 2015 Jan 16. [Epub ahead of print]

112. Deficient PKR in RAX/PKR Association Ameliorates Ethanol-Induced Neurotoxicity in the Developing Cerebellum.
Li H, Chen J, Qi Y, Dai L, Zhang M, Frank JA, Handshoe JW, Cui J, Xu W, Chen G. (USA)

ABSTRACT
Ethanol-induced neuronal loss is closely related to the pathogenesis of fetal alcohol spectrum disorders. The cerebellum is one of the brain areas that are most sensitive to ethanol. The mechanism underlying ethanol neurotoxicity remains unclear. Our previous in vitro studies have shown that the double-stranded RNA (dsRNA)-activated protein kinase (PKR) regulates neuronal apoptosis upon ethanol exposure and ethanol activates PKR through association with its intracellular activator RAX. However, the role of PKR and its interaction with RAX in vivo have not been investigated. In the current study, by utilizing N-PKR/- mice, C57BL/6J mice with a deficient RAX-binding domain in PKR, we determined the critical role of RAX/PKR association in PKR-regulated ethanol neurotoxicity in the developing cerebellum. Our data indicate that while N-PKR/- mice have a similar BAC profile as wild-type mice, ethanol induces less brain/body mass reduction as well as cerebellar neuronal loss. In addition, ethanol promotes interleukin-1β (IL-1β) secretion, and IL-1β is a master cytokine regulating inflammatory response. Importantly, ethanol-promoted IL-1β secretion is inhibited in the developing cerebellum of N-PKR/- mice. Thus, RAX/PKR interaction and PKR activation regulate ethanol neurotoxicity in the developing cerebellum, which may involve ethanol-induced neuroinflammation. Further, PKR could be a possible target for pharmacological intervention to prevent or treat fetal alcohol spectrum disorder (FASD).

Read Full Article

Hum Exp Toxicol. 2015 Jan 6. pii: 0960327114566827. [Epub ahead of print]

113. PCDHB14- and GABRB1-like nervous system developmental genes are altered during early neuronal differentiation of NCCIT cells treated with ethanol.
Halder D, Mandal C, Lee B, Lee J, Choi M, Chai J, Lee Y, Jung K, Chai Y. (Republic of Korea); ygchai@hanyang.ac.kr, khjung2@gmail.com

ABSTRACT
Ethanol (EtOH) exposure during embryonic development causes dysfunction of the central nervous system (CNS). Here, we examined the effects of chronic EtOH on gene expression during early stages of neuronal differentiation. Human embryonic carcinoma (NCCIT) cells were differentiated into neuronal precursors/lineages in the presence or absence of EtOH and folic acid. Gene expression profiling and pathway analysis demonstrated that EtOH deregulates many genes and pathways that are involved in early brain development. EtOH exposure downregulated several
important genes, such as PCDHB14, GABRB1, CTNND2, NAV3, RALDH1, and OPN5, which are involved in CNS development, synapse assembly, synaptic transmission, and neurotransmitter receptor activity. GeneGo pathway analysis revealed that the deregulated genes mapped to disease pathways that were relevant to fetal alcohol spectrum disorders (FASD, such as neurotic disorders, epilepsy, and alcohol-related disorders). In conclusion, these findings suggest that the impairment of the neurological system or suboptimal synapse formation resulting from EtOH exposure could underlie the neurodevelopmental disorders in individuals with FASD.

Read Full Article

Back to Table of Contents

114. Familiäre Belastungen in Pflege- und Adoptionsfamilien mit Kindern mit fetalem Alkoholsyndrom. [Article in German]
Sarimski K.

ABSTRACT
Abstract Caregiver Stress in Foster and Adoptive Parents of Children with Fetal Alcohol Spectrum Disorders. Foster and adoptive parents of 71 children with fetal alcohol syndrome (FAS) report on developmental and behavioral characteristics, family stress, coping resources and their satisfaction with support. The data reveal an elevated rate of social and emotional problems in the children. In spite positive individual and social resources, the foster and adoptive parents feel a high level of caregiver stress. 30 % of them rate the support they receive from pediatric, therapeutic or educational services as lower than expected. Specifically, they miss early information on the diagnosis, professional knowledge and support for the special challenges of education and managing behavioral problems in their collaboration with social support agencies.

Read Full Article

Back to Table of Contents


115. Effect of lipid raft disruption on ethanol inhibition of L1 adhesion.
Dou X, Charness ME. (USA)

ABSTRACT
BACKGROUND:
Alcohol causes fetal alcohol spectrum disorders in part by disrupting the function of the neural cell adhesion molecule L1. Alcohol inhibits L1-mediated cell-cell adhesion in diverse cell types and inhibits L1-mediated neurite outgrowth in cerebellar granule neurons (CGNs). A recent report indicates that ethanol (EtOH) induces the translocation of L1 into CGN lipid rafts and that disruption of lipid rafts prevents EtOH inhibition of L1-mediated neurite outgrowth. The same butanol-pentanol cutoff was noted for alcohol-induced translocation of L1 into lipid rafts that was reported previously for alcohol inhibition of L1 adhesion, suggesting that EtOH might inhibit L1 adhesion by shifting L1 into lipid rafts.

METHODS:
The NIH/3T3 cell line, 2A2-L1s, is a well-characterized EtOH-sensitive clonal cell line that stably expresses human L1. Cells were treated with 25 mM EtOH, 5 μM filipin, or both. Lipid rafts were enriched in membrane fractions by preparation of detergent-resistant membrane (DRMs) fractions.
Caveolin-1 was used as a marker of lipid rafts, and L1 and Src were quantified by Western blotting in lipid-raft-enriched membrane fractions and by immunohistochemistry.

RESULTS:
EtOH (25 mM) increased the percentage of L1, but not Src, in 2A2-L1s membrane fractions enriched in lipid rafts. Filipin, an agent known to disrupt lipid rafts, decreased the percentage of caveolin and L1 in DRMs from 2A2-L1s cells. Filipin also blocked EtOH-induced translocation of L1 into lipid rafts from 2A2-L1s cells but did not significantly affect L1 adhesion or EtOH inhibition of L1 adhesion.

CONCLUSIONS:
These findings indicate that EtOH does not inhibit L1 adhesion in NIH/3T3 cells by inducing the translocation of L1 into lipid rafts.

Read Full Article


Uban KA, Comeau WL, Bodnar T, Yu WK, Weinberg J, Galea LA. (Canada); kuban@chla.usc.edu

ABSTRACT
RATIONALE:
Individuals with fetal alcohol spectrum disorder (FASD) are at increased risk for substance use disorders (SUD). In typically developing individuals, susceptibility to SUD is associated with alterations in dopamine and hypothalamic-pituitary-adrenal (HPA) systems, and their interactions. Prenatal alcohol exposure (PAE) alters dopamine and HPA systems, yet effects of PAE on dopamine-HPA interactions are unknown. Amphetamine-stress cross-sensitization paradigms were utilized to investigate sensitivity of dopamine and stress (HPA) systems, and their interactions following PAE.

METHODS:
Adult Sprague-Dawley offspring from PAE, pair-fed, and ad libitum-fed control groups were assigned to amphetamine-(1-2 mg/kg) or saline-treated conditions, with injections every other day for 15 days. Fourteen days later, all animals received an amphetamine challenge (1 mg/kg) and 5 days later, hormones were measured under basal or acute stress conditions. Amphetamine sensitization (augmented locomotion, days 1-29) and cross-sensitization with acute restraint stress (increased stress hormones, day 34) were assessed.

RESULTS:
PAE rats exhibited a lower threshold for amphetamine sensitization compared to controls, suggesting enhanced sensitivity of dopaminergic systems to stimulant-induced changes. Cross-sensitization between amphetamine (dopamine) and stress (HPA hormone) systems was evident in PAE, but not in control rats. PAE males exhibited increased dopamine receptor expression (medial prefrontal cortex (mPFC)) compared to controls.

CONCLUSIONS:
PAE alters induction and expression of sensitization/cross-sensitization, as reflected in locomotor, neural, and endocrine changes, in a manner consistent with increased sensitivity of dopamine and stress systems. These results provide insight into possible mechanisms that could underlie increased prevalence of SUD, as well as the impact of widely prescribed stimulant medications among adolescents with FASD.

Read Full Article
117. **Evaluation of a Multilevel and Integrated Program to Raise Awareness of the Harmful Effects of Prenatal Alcohol Exposure in a Local Community**

Bazzo S, Battistella G, Riscica P, Moino G, Marini F, Bottarel M, Dal Pozzo G, Padovan M. (Italy);
steffania.bazzo@gmail.com

**ABSTRACT**

**AIMS:**
To evaluate a multilevel program to raise awareness of the risks of prenatal exposure to alcohol in the area of Treviso (Italy). The program started in 2008 and consists of an action-research experience involving health professionals of maternal-child services, and in the campaign 'Mamma Beve Bimbo Beve', targeted to the childbearing-aged population.

**METHODS:**
A comparative study was carried out in 2013. Surveys using semi-structured self-report questionnaires were carried out among professionals and pregnant women in Treviso, and among control groups belonging to another local area of Italy (Verona). The questionnaires investigated awareness and opinions about alcohol and pregnancy, as well as sources and kind of information provided and received.

**RESULTS:**
Health professionals in Treviso, who had been exposed both to the action-research experience and to the campaign, showed a more rational approach to alcohol than colleagues in the control group, and were more aware and sensitized about the risks of alcohol consumption during pregnancy. Physicians and midwives had a higher probability of having advised pregnant women to abstain from alcohol in Treviso. Pregnant women in Treviso, who had received information through the campaign and from professionals, had a higher probability of having received only correct advice about the issue of alcohol and pregnancy, but did not hold perceptions different to women in Verona.

**CONCLUSIONS:**
The multilevel program carried out in the Treviso area was effective in increasing awareness and improving attitudes towards the risks of alcohol use during pregnancy among local healthcare professionals, compared with the control group.

Read Full Article

**Back to Table of Contents**

---

118. **Effects of developmental alcohol exposure vs. intubation stress on BDNF and TrkB expression in the hippocampus and frontal cortex of neonatal rats.**

Boschen KE, Criss KJ, Palamarchouk V, Roth TL, Klintsova AY. (USA); klintsov@udel.edu

**ABSTRACT**

Third trimester-equivalent alcohol exposure causes significant deficits in hippocampal and corticarneuroplasticity, resulting in alterations to dendritic arborization, hippocampal adult neurogenesis, and performance on learning tasks. The current study investigated the impact of neonatal alcoholecexposure (postnatal days 4-9, 5.25g/kg/day) on expression of brain-derived neurotrophic factor (BDNF) and the tropomysin-related kinase B (TrkB) receptor in the hippocampal and frontal cortex of infant Long-Evans rats. Levels of BDNF protein were increased in the hippocampus, but not frontal cortex, of alcohol-exposed rats 24h after the last dose, when compared with undisturbed (but not sham-intubated) control animals. BDNF protein levels showed a trend toward increase in hippocampus of sham-intubated animals as well, suggesting an effect of the intubation procedure. TrkB protein was increased in the hippocampus of alcohol-exposed
animals compared to sham-intubated pups, indicating an alcohol-specific effect on receptor expression. In addition, expression of bdnf total mRNA in alcohol-exposed and sham-intubated pups was enhanced in the hippocampus; however, there was a differential effect of alcohol and intubation stress on exon I- and IV-specific mRNA transcripts. Further, plasma corticosterone was found to be increased in both alcohol-exposed and sham-intubated pups compared to undisturbed animals. Upregulation of BDNF could potentially represent a neuroprotective mechanism activated following alcohol exposure or stress. The results suggest that alcohol exposure and stress have both overlapping and unique effects on BDNF, and highlight the need for the stress of intubation to be taken into consideration in studies that implement this route of drug delivery.

Read Full Article

119. Prenatal alcohol exposure and adolescent stress increase sensitivity to stress and gonadal hormone influences on cognition in adult female rats.
Comeau WL, Lee K, Anderson K, Weinberg J. (Canada); comeauwe@mail.ubc.ca

ABSTRACT
Abnormal activity of stress hormone (hypothalamic-pituitary-adrenal [HPA]), and gonadal hormone (hypothalamic-pituitary-gonadal [HPG]) systems is reported following prenatal alcohol exposure (PAE). PAE increases vulnerability of brain regions involved in regulation of these systems to stressors or challenges during sensitive periods of development, such as adolescence. In addition, HPA and HPG functions are linked to higher order functions such as executive function (EF), with dysregulation of either system adversely affecting EF processes, including attention and response inhibition, that influence cognition. However, how HPA and HPG systems interact to influence cognitive performance in individuals with an FASD is not fully understood. To investigate, we used a rat model of moderate PAE. Adolescent female PAE and control offspring were exposed to 10 days of chronic mild stress (CMS) and cognitive function was assessed on the radial arm maze (RAM) in adulthood. On the final test day, animals were sacrificed, with blood collected for hormone analyses, and vaginal smears taken to assess estrus stage at the time of termination. Analyses showed that adolescent CMS significantly increased levels of CORT and RAM errors during proestrus in adult PAE but not control females. Moreover, CORT levels were correlated with estradiol levels and with RAM errors, but only in PAE females, with outcome dependent on adolescent CMS condition. These results suggest that PAE increases sensitivity to the influences of stress and gonadal hormones on cognition, and thus, in turn, that HPA and HPG dysregulation may underlie some of the deficits in executive function described previously in PAE females.

Read Full Article

120. Dissecting FASD through the global transcriptome.
Zhou FC. (USA)


Read Full Article

Koren G. (Canada); gkoren@sickkids.ca

ABSTRACT
Fetal alcohol spectrum disorder (FASD) is considered to be the most common cause of developmental disability, affecting more than 1% of the general population in North America. Inattention, hyperactivity, and impulsivity afflict 50-90% of children with FASD and are 3-9 times more common than in the general population. Of importance, a large proportion of children with FASD are affected by oppositional defiant/conduct disorder (ODD/CD), including lack of social judgment and failure to learn from experience. These devastating numbers are contrasted by almost no pharmacological research into treatment of these pervasive conditions in FASD. This review focuses on analyzing the published evidence on the effectiveness and safety of therapy for disruptive behaviors in FASD. Often, the child afflicted by FASD will not be allowed to participate in class activities without such therapies, which makes such analysis critical.

Read Full Article

Back to Table of Contents


122. Apoptotic cell death and temporal expression of apoptotic proteins Bcl-2 and Bax in the hippocampus, following binge ethanol in the neonatal rat model.

Smith CC, Guévremont D, Williams JM, Napper RM. (New Zealand)

ABSTRACT
BACKGROUND:
Binge-like ethanol (EtOH) exposure during the early rat neonatal period results in acute cell loss in specific brain regions, but such acute cell death has not been well established in the hippocampus. Binge alcohol exposure can also result in protein expression changes in the cerebellum that could alter cell fate, but this has not been reported for the hippocampal subregions. This study investigates acute apoptotic cell death in hippocampal regions CA1, CA3, and dentate gyrus (DG) following a binge EtOH exposure on postnatal day (PN) 6, PN8, or PN6 + 8 and the alteration in pro- and anti-apoptotic proteins following a single EtOH binge on PN6.

METHODS:
Apoptotic cell death was quantified 12 hours after EtOH binge exposure using the optical fractionator method. Western blot analysis determined expression of pro-apoptotic Bax and anti-apoptotic Bcl-2, 12, 24, and 48 hours after binge EtOH exposure on PN6. The Bcl-2:Bax ratio was used as a measure of vulnerability to apoptosis.

RESULTS:
Acute apoptosis increased significantly 12 hours following PN6 or 8 EtOH exposure in CA1, CA3, and DG, but the magnitude of apoptotic cell death was significantly greater in CA1 than in CA3 and DG, which did not differ. Significant cell death was not detected when a PN8 EtOH exposure was preceded by exposure on PN6. Binge EtOH exposure on PN6 resulted in a significant increase in expression of Bcl-2 and the Bcl-2:Bax ratio in the CA1/DG region at 24 hours after EtOH exposure on PN6. The Bcl-2:Bax ratio in the CA3 region was not altered.

CONCLUSIONS:
This study shows that repeated binge exposure does not have a cumulative effect on the magnitude of acute apoptotic cell death. This finding may be explained in part by changes in the Bcl-2:Bax ratio after a single binge EtOH exposure.

www.nofas-uk.org
123. Ethanol exposure during gastrulation alters neuronal morphology and behavior in zebrafish.
Shan SD, Boutin S, Ferdous J, Ali DW. (Canada); declan.ali@ualberta.ca

ABSTRACT
Ethanol (EtOH) exposure during development has been shown to lead to deficits in fine and gross motor control. In this study we used zebrafish embryos to determine the effects of EtOH treatment during gastrulation. We treated embryos in the gastrulation stage (5.25 hours post fertilization (hpf) to 10.75 hpf) with 10 mM, 50 mM or 100 mM EtOH and examined the effects on general animal morphology, the c-start reflex behavior, Mauthner cell (M-cell) morphology and motor neuron morphology. EtOH treated fish exhibited a minor but significant increase in gross morphological deformities compared with untreated fish. Behavioral studies showed that EtOH treatment resulted in an increase in the peak speed of the tail during the escape response. Furthermore, there was a marked increase in abnormally directed c-starts, with treated fish showing greater incidences of c-starts in inappropriate directions. Immunolabeling of the M-cells, which are born during gastrulation, revealed that they were significantly smaller in fish treated with 100 mM EtOH compared with controls. Immunolabeling of primary motor neurons using anti-znp1, showed no significant effect on axonal branching, whereas secondary motor axons had a greater number of branches in ethanol treated fish compared with controls. Together these findings indicate that ethanol exposure during gastrulation can lead to alterations in behavior, neuronal morphology and possibly function.

124. Looking further upstream to prevent fetal alcohol spectrum disorder in Canada.
Sanders J, Currie CL. (Canada); james.sanders@uleth.ca

ABSTRACT
Half of all pregnancies in Canada are unintended. Whether a pregnancy is intended or unintended has a bearing on the risk of prenatal alcohol exposure. Research indicates that women who experience an unintended pregnancy are significantly more likely to consume alcohol while pregnant. Most fetal alcohol spectrum disorder (FASD) prevention frameworks in Canada have adopted a mid-stream approach focused on preventing alcohol consumption among women who are already pregnant. Yet there is a second approach, further upstream, that is rarely discussed as an FASD prevention tool in this country - preventing unintended pregnancy itself. Improving access to long-acting reversible contraceptives for women and girls who are experiencing cost and access barriers to these methods could do much to stem the incidence of FASD and the prohibitive health and social costs associated with this disorder in Canada.

125. Zebrafish retinal defects induced by ethanol exposure are rescued by retinoic acid and folic acid supplement.
Muralidharan P, Sarmah S, Marrs JA. (USA); jmarrs@iu.edu
ABSTRACT
Fetal Alcohol Spectrum Disorder (FASD) is caused by prenatal alcohol exposure, producing craniofacial, sensory, motor, and cognitive defects. FASDs are highly prevalent in low socioeconomic populations, which are frequently accompanied by malnutrition. FASD-associated ocular pathologies include microphthalmia, optic nerve hypoplasia, and cataracts. The present study characterizes specific retinal tissue defects, identifies ethanol-sensitive stages during retinal development, and dissects the effect of nutrient supplements, such as retinoic acid (RA) and folic acid (FA) on ethanol-induced retinal defects. Exposure to pathophysiological concentrations of ethanol (during midblastula transition through somitogenesis; 2-24 h post fertilization [hpf]) altered critical transcription factor expression involved in retinal cell differentiation, and produced severe retinal ganglion cell, photoreceptor, and Müller glial differentiation defects. Ethanol exposure did not alter retinal cell differentiation induction, but increased retinal cell death and proliferation. RA and FA nutrient co-supplementation rescued retinal photoreceptor and ganglion cell differentiation defects. Ethanol exposure during retinal morphogenesis stages (16-24 hpf) produced retinal defects like those seen with ethanol exposure between 2 and 24 hpf. Significantly, during an ethanol-sensitive time window (16-24 hpf), RA co-supplementation moderately rescued these defects, whereas FA co-supplementation showed significant rescue of optic nerve and photoreceptor differentiation defects. Interestingly, RA, but not FA, supplementation after ethanol exposure could reverse ethanol-induced optic nerve and photoreceptor differentiation defects. Our results indicate that various ethanol-sensitive events underlie FASD-associated retinal defects. Nutrient supplements like retinoids and folate were effective in alleviating ethanol-induced retinal defects.

Read Full Article
Back to Table of Contents

126. Gypenosides protected the neural stem cells in the subventricular zone of neonatal rats that were prenatally exposed to ethanol.
Dong L, Yang KQ, Fu WY, Shang ZH, Zhang QY, Jing FM, Li LL, Xin H, Wang XJ. (China);
luckwang@sdu.edu.cn

ABSTRACT
Fetal alcohol spectrum disorder (FASD) can cause severe mental retardation in children who are prenatally exposed to ethanol. The effects of prenatal and early postnatal ethanol exposure on adult hippocampal neurogenesis have been investigated; however, the effects of prenatal ethanol exposure on the subventricular zone (SVZ) have not. Gypenosides (GPs) have been reported to have neuroprotective effects in addition to other bioactivities. The effects of GPs on neural stem cells (NSCs) in the FASD model are unknown. Here, we test the effect of prenatal ethanol exposure on the neonatal SVZ, and the protection potential of GPs on NSCs in FASD rats. Our results show that prenatal ethanol exposure can suppress the cell proliferation and differentiation of neural stem cells in the neonatal SVZ and that GPs (400 mg/kg/day) can significantly increase the cell proliferation and differentiation of neural stem cells inhibited by ethanol. Our data indicate that GPs have neuroprotective effects on the NSCs and can enhance the neurogenesis inhibited by ethanol within the SVZ of neonatal rats. These findings provide new evidence for a potential therapy involving GPs for the treatment of FASD.

Read Full Article
Back to Table of Contents

127. Pre- and postnatal exposure to moderate levels of ethanol can have long-lasting effects on hippocampal glutamate uptake in adolescent offspring.
Brolese G, Lunardi P, de Souza DF, Lopes FM, Leite MC, Gonçalves CA. (Brazil)
ABSTRACT
The developing brain is vulnerable to the effects of ethanol. Glutamate is the main mediator of excitatory signals in the brain and is probably involved in most aspects of normal brain function during development. The aim of this study was to investigate vulnerability to and the impact of ethanol toxicity on glutamate uptake signaling in adolescent rats after moderate pre and postnatal ethanol exposure. Pregnant female rats were divided into three groups and treated only with water (control), non-alcoholic beer (vehicle) or 10% (v/v) beer solution (moderate prenatal alcohol exposure-MPAE). Thirty days after birth, adolescent male offspring were submitted to hippocampal acute slice procedure. We assayed glutamate uptake and measured glutathione content and also quantified glial glutamate transporters (EAAT 1 and EAAT 2). The glutamate system vulnerability was tested with different acute ethanol doses in naïve rats and compared with the MPAE group. We also performed a (lipopolysaccharide-challenge (LPS-challenge) with all groups to test the glutamate uptake response after an insult. The MPAE group presented a decrease in glutamate uptake corroborating a decrease in glutathione (GSH) content. The reduction in GSH content suggests oxidative damage after acute ethanol exposure. The glial glutamate transporters were also altered after prenatal ethanol treatment, suggesting a disturbance in glutamate signaling. This study indicates that impairment of glutamate uptake can be dose-dependent and the glutamate system has a higher vulnerability to ethanol toxicity after moderate ethanol exposure In utero. The effects of pre- and postnatal ethanol exposure can have long-lasting impacts on the glutamate system in adolescence and potentially into adulthood.

Read Full Article
Back to Table of Contents

128. Correlates of partner support to abstain from prenatal alcohol use: a cross-sectional survey among Dutch partners of pregnant women.
van der Wulp NY1, Hoving C, de Vries H. (The Netherlands)

ABSTRACT
Partners can play an important role, but are often ignored in interventions targeting the prevention of prenatal alcohol use. A better understanding of the correlates of partner support to abstain from prenatal alcohol use can help to make a better use of partner support. The aim of this study was to identify correlates of this support by analysing differences between partners reporting low versus high support. An online cross-sectional study among 237 Dutch partners of pregnant women was conducted. Respondents were recruited through Dutch midwifery practices in September-October 2009. Questionnaires were based on the I-Change Model. Chi-square and t-test showed that partners reporting high support were more likely to desire their partner to abstain from alcohol use and to have received advice from their pregnant spouse or midwife that abstinence was desirable. They also had stronger perceptions that the baby would experience harm from prenatal alcohol use and that harm could be more severe, and they saw more advantages and fewer disadvantages of providing support. They also reported more influence from their social environment encouraging their support, had greater self-efficacy and had a stronger intention to support their partner during the remainder of the pregnancy compared to partners reporting low support. Health professionals may improve their alcohol advice by discussing the advantages and disadvantages of support with the partner and by encouraging couples to discuss and propose solutions for the situations in which partners find it difficult not to support alcohol abstinence. By providing an insight into important correlates of partner support, this study expands the research area aiming to reduce prenatal alcohol use.

Read Full Article
Back to Table of Contents
ABSTRACT

OBJECTIVE:
To investigate the effects of prenatal alcohol exposure on rhythmic respiratory discharge activity (RRDA) in the medullary slices of neonatal rats.

METHODS:
Ten pregnant female SD rats were exposed to 0, 4%, 6%, 8%, and 10% alcohol in drinking water from 1 week before till 3 days after delivery. The medullary slices of the neonatal rats containing the medial region of the nucleus retrofacialis (mNRF) with the hypoglossal nerve rootlets were prepared and perfused with modified Kreb's solution to record RRDA from the hypoglossal nerve rootlets using suction electrodes.

RESULTS:
No significant difference was found in RRDA in 50 min among the neonatal rats with prenatal exposure to 0, 4%, 6%, and 8% alcohol, but the RRDA in 10% alcohol exposure group became irregular. Prenatal exposure to increased alcohol concentrations caused attenuated RRDA attenuated in the neonatal rats, shown by shortened inspiratory time (TI), decreased respiratory frequency (RF), and reduced integral amplitude (IA) as compared with those in the control group.

CONCLUSION:
Prenatal alcohol exposure inhibits RRDA in medullary slices of neonatal rats, which might be a mechanism by which maternal alcohol exposure causes suppressed offspring respiratory functions.

Read Full Article

Back to Table of Contents
cells (and of these cells more immature proliferating cells but fewer postmitotic cells) than nulliparous females. Collectively, these data suggest that alcohol consumption during pregnancy disrupts maternal care without affecting HPA function or neurogenesis in dams. Conversely, alcohol altered HPA function in nulliparous females only, suggesting that reproductive experience buffers the long-term effects of alcohol on the HPA axis.

Read Full Article
Back to Table of Contents


131. In Utero exposure to low-dose alcohol induces reprogramming of mammary development and tumor risk in MMTV-erbB-2 transgenic mice.
Ma Z, Blackwelder AJ, Lee H, Zhao M, Yang X. (USA); xyang@nccu.edu

ABSTRACT
There is increasing evidence that prenatal exposure to environmental factors may modify breast cancer risk later in life. This study aimed to investigate the effects of in utero exposure to low-dose alcohol on mammary development and tumor risk. Pregnant MMTV-erbB-2 mice were exposed to alcohol (6 g/kg/day) between day 13 and day 19 of gestation, and the female offspring were examined for tumor risk. Whole mount analysis indicated that in utero exposure to low-dose alcohol induced significant increases in ductal extension at 10 weeks of age. Molecular analysis showed that in utero alcohol exposure induced upregulation of ERα signaling and activation of Akt and Erk1/2 in pubertal mammary glands. However, enhanced signaling in the EGFR/erbB-2 pathway appeared to be more prominent in 10-week-old glands than did signaling in the other pathways. Interestingly, tumor development in mice with in utero exposure to low-dose alcohol was slightly delayed compared to control mice, but tumor multiplicity was increased. The results indicate that in utero exposure to low-dose alcohol induces the reprogramming of mammary development by mechanisms that include altered signaling in the estrogen receptor (ER) and erbB-2 pathways. The intriguing tumor development pattern might be related to alcohol dose and exposure conditions, and warrants further investigation.

Read Full Article
Back to Table of Contents


132. Prenatal ethanol increases ethanol intake throughout adolescence, alters ethanol-mediated aversive learning, and affects μ but not δ or κ opioid receptor mRNA expression.
Fabio MC, Macchione AF, Nizhnikov ME, Pautassi RM. (Argentina)

ABSTRACT
Animal models of prenatal ethanol exposure (PEE) have indicated a facilitatory effect of PEE on adolescent ethanol intake, but few studies have assessed the effects of moderate PEE throughout adolescence. The mechanisms underlying this facilitatory effect remain largely unknown. In the present study, we analysed ethanol intake in male and female Wistar rats with or without PEE (2.0 g/kg, gestational days 17-20) from postnatal days 37 to 62. The results revealed greater ethanol consumption in PEE rats than in controls, which persisted throughout adolescence. By the end of testing, ethanol ingestion in PEE rats was nearly 6.0 g/kg. PEE was associated with insensitivity to ethanol-induced aversion. PEE and control rats were further analysed for levels of μ, δ and κ opioid receptor mRNA in the infralimbic cortex, nucleus accumbens shell, and ventral tegmental area. Similar levels of mRNA were observed across most areas and opioid receptors, but...
μ receptor mRNA in the ventral tegmental area was significantly increased by PEE. Unlike previous studies that assessed the effects of PEE on ethanol intake close to birth, or in only a few sessions during adolescence, the present study observed a facilitatory effect of PEE that lasted throughout adolescence. PEE was associated with insensitivity to the aversive effect of ethanol, and increased levels of μ opioid receptor transcripts. PEE is a prominent vulnerability factor that probably favors the engagement of adolescents in risky trajectories of ethanol use.

Read Full Article
Back to Table of Contents


133. Effects of ethanol exposure in utero on Cajal-Retzius cells in the developing cortex.
Skorput AG, Yeh HH. (Lebanon, USA)

ABSTRACT
BACKGROUND:
Prenatal exposure to ethanol exerts teratogenic effects on the developing brain. Here, we tested the hypothesis that exposure to ethanol in utero alters the disposition of Cajal-Retzius cells that play a key role in orchestrating proliferation, migration, and laminar integration of cortical neurons in the embryonic cortex.

METHODS:
Pregnant Ebf2-EGFP mice, harboring EGFP-fluorescent Cajal-Retzius cells, were subjected to a 2% w/w ethanol consumption regimen starting at neural tube closure and lasting throughout gestation. Genesis of Cajal-Retzius cells was assessed by means of 5-bromo-2-deoxyuridine (BrdU) immunofluorescence at embryonic day 12.5, their counts and distribution were determined between postnatal day (P)0 and P4, patch clamp electrophysiology was performed between P2 and P3 to analyze GABA-mediated synaptic activity, and open-field behavioral testing was conducted in P45-P50 adolescents.

RESULTS:
In Ebf2-EGFP embryos exposed to ethanol in utero, we found increased BrdU labeling and expanded distribution of Cajal-Retzius cells in the cortical hem, pointing to increased genesis and proliferation. Postnatally, we found an increase in Cajal-Retzius cell number in cortical layer I. In addition, they displayed altered patterning of spontaneous GABA-mediated synaptic barrages and enhanced GABA-mediated synaptic activity, suggesting enhanced GABAergic tone.

CONCLUSIONS:
These findings, together, underscore that Cajal-Retzius cells contribute to the ethanol-induced aberration of cortical development and abnormal GABAergic neurotransmission at the impactful time when intracortical circuits form.

Read Full Article
Back to Table of Contents


134. The impact of prenatal alcohol exposure on hippocampal-dependent outcome measures is influenced by prenatal and early-life rearing conditions.
Caldwell KK, Goggin SL, Labrecque MT, Allan AM. (USA)
ABSTRACT

BACKGROUND:
The clinical course of individuals exposed to alcohol in utero is influenced by multiple factors, including the social environments of the gravid female and offspring. In the present studies we focused on the effects of prenatal alcohol exposure (PAE) and the prenatal and early-life social environments on the hippocampal formation, as impaired development and functioning of this brain region have been implicated in several of the adverse cognitive outcomes associated with PAE.

METHODS:
We combined our PAE mouse model with 2 conditions of housing pregnant dams and their preweaning offspring: the standard nest (SN), in which a dam is individually housed prior to parturition and then remains isolated with her offspring, and the communal nest (CN), in which multiple dams are housed together prior to parturition and then following delivery the moms and their litters share a nest. Mouse dams consumed either 10% (w/v) ethanol in 0.066% (w/v) saccharin (SAC) or 0.066% (w/v) SAC alone using a limited (4-hour) access, drinking-in-the-dark paradigm. Immunoblotting techniques were used to measure levels of the glucocorticoid receptor (GR), 11β-hydroxysteroid dehydrogenase 1, the FK506-binding proteins 51 and 52, and corticotropin-releasing hormone receptor type 1 in the hippocampal formation isolated from male adolescent offspring. We also determined the effect of PAE and rearing conditions on context discrimination, a hippocampal-dependent learning/memory task.

RESULTS:
SN PAE offspring displayed impaired context discrimination and neurochemical changes in the hippocampal formation consistent with increased GR nuclear localization. These effects of PAE were, in general, ameliorated in mice reared in a CN. The CN also altered neurochemical measures and improved learning/memory in SAC control animals.

CONCLUSIONS:
These studies demonstrate a complex interplay between the effects of PAE and social environments. The findings have important translational implications, as well as highlight the importance of considering rearing conditions in the interpretation of research findings on PAE.

Read Full Article
Back to Table of Contents


135. Moderate prenatal alcohol exposure enhances GluN2B containing NMDA receptor binding and ifenprodil sensitivity in rat agranular insular cortex.

Bird CW, Candelaria-Cook FT, Magcalas CM, Davies S, Valenzuela CF, Savage DD, Hamilton DA. (USA)

ABSTRACT
Prenatal exposure to alcohol affects the expression and function of glutamatergic neurotransmitter receptors in diverse brain regions. The present study was undertaken to fill a current gap in knowledge regarding the regional specificity of ethanol-related alterations in glutamatergic receptors in the frontal cortex. We quantified subregional expression and function of glutamatergic neurotransmitter receptors (AMPARs, NMDARs, GluN2B-containing NMDARs, mGluR1s, and mGluR5s) by radioligand binding in the agranular insular cortex (AID), lateral orbital area (LO), prelimbic cortex (PrL) and primary motor cortex (M1) of adult rats exposed to moderate levels of ethanol during prenatal development. Increased expression of GluN2B-containing NMDARs was observed in AID of ethanol-exposed rats compared to modest reductions in other regions. We subsequently performed slice electrophysiology measurements in a whole-cell patch-clamp preparation to quantify the sensitivity of evoked NMDAR-mediated excitatory postsynaptic currents (EPSCs) in layer II/III pyramidal neurons of AID to the GluN2B negative allosteric modulator ifenprodil. Consistent with increased GluN2B expression, ifenprodil caused a greater reduction in
NMDAR-mediated EPSCs from prenatal alcohol-exposed rats than saccharin-exposed control animals. No alterations in AMPAR-mediated EPSCs or the ratio of AMPARs/NMDARs were observed. Together, these data indicate that moderate prenatal alcohol exposure has a significant and lasting impact on GluN2B-containing receptors in AID, which could help to explain ethanol-related alterations in learning and behaviors that depend on this region.

Read Full Article
Back to Table of Contents

Lussier AA, Stepien KA, Neumann SM, Pavlidis P, Kobor MS, Weinberg J. (Canada)

ABSTRACT
BACKGROUND:
Prenatal alcohol exposure (PAE) is associated with alterations in numerous physiological systems, including the stress and immune systems. We have previously shown that PAE increases the course and severity of arthritis in an adjuvant-induced arthritis (AA) model. While the molecular mechanisms underlying these effects are not fully known, changes in neural gene expression are emerging as important factors in the etiology of PAE effects. As the prefrontal cortex (PFC) and hippocampus (HPC) play key roles in neuroimmune function, PAE-induced alterations to their transcriptome may underlie abnormal steady-state functions and responses to immune challenge. This study examined brains from adult PAE and control females from our recent AA study to determine whether PAE causes long-term alterations in gene expression and whether these mediate the altered severity and course of arthritis in PAE females.

METHODS:
Adult females from PAE, pair-fed (PF), and ad libitum-fed control (C) groups were injected with either saline or complete Freund's adjuvant. Animals were terminated at the peak of inflammation or during resolution (Days 16 and 39 postinjection, respectively); cohorts of saline-injected PAE, PF, and C females were terminated in parallel. Gene expression was analyzed in the PFC and HPC using whole-genome mRNA expression microarrays.

RESULTS:
Significant changes in gene expression in both the PFC and HPC were found in PAE compared to controls in response to ethanol exposure alone (saline-injected females), including genes involved in neurodevelopment, apoptosis, and energy metabolism. Moreover, in response to inflammation (adjuvant-injected females), PAE animals showed unique expression patterns, while failing to exhibit the activation of genes and regulators involved in the immune response observed in control and pair-fed animals.

CONCLUSIONS:
These results support the hypothesis that PAE affects neuroimmune function at the level of gene expression, demonstrating long-term effects of PAE on the central nervous system response under steady-state conditions and following an inflammatory insult.

Read Full Article
Back to Table of Contents
Glass L, Graham DM, Akshoomoff N, Mattson SN.

ABSTRACT

OBJECTIVE:
Heavy prenatal alcohol exposure is associated with impaired school functioning. Spelling performance has not been comprehensively evaluated. We examined whether children with heavy prenatal alcohol exposure demonstrate deficits in spelling and related abilities, including reading, and tested whether there are unique underlying mechanisms for observed deficits in this population.

METHODS:
Ninety-six school-age children made up 2 groups: children with heavy prenatal alcohol exposure (AE, n = 49) and control children (CON, n = 47). Children completed select subtests from the Wechsler Individual Achievement Test-Second Edition and the NEPSY-II. Group differences and relations between spelling and theoretically related cognitive variables were evaluated using multivariate analysis of variance and Pearson correlations. Hierarchical regression analyses were used to assess contributions of group membership and cognitive variables to spelling performance. The specificity of these deficits and underlying mechanisms was tested by examining the relations between reading ability, group membership, and cognitive variables.

RESULTS:
Groups differed significantly on all variables. Group membership and phonological processing significantly contributed to spelling performance, whereas for reading, group membership and all cognitive variables contributed significantly. For both reading and spelling, group × working memory interactions revealed that working memory contributed independently only for alcohol-exposed children.

CONCLUSIONS:
Alcohol-exposed children demonstrated a unique pattern of spelling deficits. The relation of working memory to spelling and reading was specific to the AE group, suggesting that if prenatal alcohol exposure is known or suspected, working memory ability should be considered in the development and implementation of explicit instruction.

Read Full Article
Back to Table of Contents


ABSTRACT

BACKGROUND:
Alcohol exposure has adverse effects on stress physiology and behavioral reactivity. This is suggested to be due, in part, to the effect of alcohol on β-endorphin (β-EP)-producing neurons in the hypothalamus. In response to stress, β-EP normally provides negative feedback to the hypothalamic-pituitary-adrenal axis and interacts with other neurotransmitter systems in the amygdala to regulate behavior. We examined whether β-EP neuronal function in the hypothalamus reduces the corticosterone response to acute stress, attenuates anxiety-like behaviors, and modulates alcohol drinking in rats.

www.nofas-uk.org 150
METHODS:
To determine whether β-EP neuronal transplants modulate the stress response, anxiety behavior, and alcohol drinking, we implanted differentiated β-EP neurons into the paraventricular nucleus (PVN) of the hypothalamus of normal, prenatal alcohol-exposed, and alcohol-preferring (P) and alcohol-non-preferring (NP) rats. We then assessed corticosterone levels in response to acute restraint stress and other markers of stress response in the brain and anxiety-like behaviors in the elevated plus maze and open-field assays.

RESULTS:
We showed that β-EP neuronal transplants into the PVN reduced the peripheral corticosterone response to acute stress and attenuated anxiety-like behaviors. Similar transplants completely reduced the hypercorticosterone response and elevated anxiety behaviors in prenatal alcohol-exposed adult rats. Moreover, we showed that β-EP reduced anxiety behavior in P rats with minimal effects on alcohol drinking during and following restraint stress.

CONCLUSIONS:
These data further establish a role of β-EP neurons in the hypothalamus for regulating physiological stress response and anxiety behavior and resemble a potential novel therapy for treating stress-related psychiatric disorders in prenatal alcohol-exposed children and those genetically predisposed to increased alcohol consumption.

Read Full Article
Back to Table of Contents


139. Clinical sensitivity and specificity of meconium fatty acid ethyl ester, ethyl glucuronide, and ethyl sulfate for detecting maternal drinking during pregnancy.
Himes SK, Dukes KA, Tripp T, Petersen JM, Raffo C, Burd L, Odendaal H, Elliott AJ, Hereld D, Signore C, Willinger M, Huestis MA; Prenatal Alcohol in SIDS and Stillbirth (PASS) Network. (USA);
mhuestis@intra.nida.nih.gov

ABSTRACT
BACKGROUND:
We investigated agreement between self-reported prenatal alcohol exposure (PAE) and objective meconium alcohol markers to determine the optimal meconium marker and threshold for identifying PAE.

METHODS:
Meconium fatty acid ethyl esters (FAEE), ethyl glucuronide (EtG), and ethyl sulfate (EtS) were quantified by LC-MS/MS in 0.1 g meconium from infants of Safe Passage Study participants. Detailed PAE information was collected from women with a validated timeline follow-back interview. Because meconium formation begins during weeks 12-20, maternal self-reported drinking at or beyond 19 weeks was our exposure variable.

RESULTS:
Of 107 women, 33 reported no alcohol consumption in pregnancy, 16 stopped drinking by week 19, and 58 drank beyond 19 weeks (including 45 third-trimester drinkers). There was moderate to substantial agreement between self-reported PAE at ≥19 weeks and meconium EtG ≥30 ng/g (κ = 0.57, 95% CI 0.41-0.73). This biomarker and associated cutoff was superior to a 7 FAEE sum ≥2 nmol/g and all other individual and combination marker cutoffs. With meconium EtG ≥30 ng/g as the gold standard condition and maternal self-report at ≥19 weeks' gestation as the test condition, 82% clinical sensitivity (95% CI 71.6-92.0) and 75% specificity (95% CI 63.2-86.8) were observed. A significant dose-concentration relationship between self-reported drinks per drinking day and meconium EtG ≥30 ng/g also was observed (all P < 0.01).
CONCLUSIONS:
Maternal alcohol consumption at ≥19 weeks was better represented by meconium EtG ≥30 ng/g than currently used FAEE cutoffs.

Read Full Article
Back to Table of Contents

140. Effects of prenatal alcohol and cigarette exposure on offspring substance use in multiplex, alcohol-dependent families.
O’Brien JW, Hill SY. (USA)

ABSTRACT

BACKGROUND:
Prenatal exposures to alcohol, cigarettes, and other drugs of abuse are associated with numerous adverse consequences for affected offspring, including increased risk for substance use and abuse. However, maternal substance use during pregnancy appears to occur more often in those with a family history of alcohol dependence. Utilizing a sample that is enriched for familial alcohol dependence and includes controls selected for virtual absence of familial alcohol dependence could provide important information on the relative contribution of familial risk and prenatal exposures to offspring substance use.

METHODS:
A sample of multigenerational families specifically ascertained to be at either high or low risk for developing alcohol dependence (AD) provided biological offspring for a longitudinal prospective study. High-risk families were selected based on the presence of 2 alcohol-dependent sisters. Low-risk families were selected on the basis of minimal first and second-degree relatives with AD. High-risk (HR = 99) and Low-risk offspring (LR = 110) were assessed annually during childhood and biennially in young adulthood regarding their alcohol, drug, and cigarette use. At the first childhood visit, mothers were interviewed concerning their prenatal use of substances.

RESULTS:
High-risk mothers were more likely to use alcohol, cigarettes, and other drugs during pregnancy than low-risk control mothers, and to consume these substances in greater quantities. Across the sample, prenatal exposure to alcohol was associated with increased risk for both offspring cigarette use and substance use disorders (SUD), and prenatal cigarette exposure was associated with increased risk for offspring cigarette use. Controlling for risk status by examining patterns within the HR sample, prenatal cigarette exposure remained a specific predictor of offspring cigarette use, and prenatal alcohol exposure was specifically associated with increased risk for offspring SUD.

CONCLUSIONS:
Women with a family history of SUD are at increased risk for substance use during pregnancy. Both familial loading for alcohol dependence and prenatal exposure to alcohol or cigarettes are important risk factors in the development of offspring substance use. An inadequate assessment of family history may obscure important interactions between familial risk and prenatal exposures on offspring outcomes.

Read Full Article
Back to Table of Contents

Moderate-level prenatal alcohol exposure induces sex differences in dopamine D1 receptor binding in adult rhesus monkeys.

Converse AK, Moore CF, Holden JE, Ahlers EO, Moirano JM, Larson JA, Resch LM, DeJesus OT, Barnhart TE, Nickles RJ, Murali D, Christian BT, Schneider ML. (USA)

ABSTRACT

BACKGROUND:
We examined the effects of moderate prenatal alcohol exposure and/or prenatal stress exposure on (D1 R) binding in a non human primate model. The dopamine D1 R is involved in executive function, and it may play a role in cognitive behavioral deficits associated with prenatal alcohol and/or stress exposure. Little is known, however, about the effects of prenatal alcohol and/or stress exposure on the D1 R. We expected that prenatal insults would lead to alterations in D1 R binding in prefrontal cortex (PFC) and striatum in adulthood.

METHODS:
Rhesus macaque females were randomly assigned to moderate alcohol exposure and/or mild prenatal stress as well as a control condition during pregnancy. Thirty-eight offspring were raised identically and studied as adults by noninvasive in vivo neuroimaging using positron emission tomography with the D1 antagonist radiotracer [(11) C]SCH 23390. Radiotracer binding in PFC and striatum was evaluated by 2 (alcohol) × 2 (stress) × 2 (sex) analysis of variance.

RESULTS:
In PFC, a significant alcohol × sex interaction was observed with prenatal alcohol exposure leading to increased [(11) C]SCH 23390 binding in male monkeys. No main effect of prenatal alcohol or prenatal stress exposure was observed.

CONCLUSIONS:
These results suggest that prenatal alcohol exposure results in long-term increases in prefrontal dopamine D1 R binding in males. This may help explain gender differences in the prevalence of neurodevelopmental disorders consequent to prenatal alcohol exposure.

Read Full Article
Back to Table of Contents

Using optical coherence tomography to rapidly phenotype and quantify congenital heart defects associated with prenatal alcohol exposure.

Karu namuni G, Gu S, Doughman YQ, Noonan AI, Rollins AM, Jenkins MW, Watanabe M. (USA)

ABSTRACT

BACKGROUND:
The most commonly used method to analyze congenital heart defects involves serial sectioning and histology. However, this is often a time-consuming process where the quantification of cardiac defects can be difficult due to problems with accurate section registration. Here we demonstrate the advantages of using optical coherence tomography, a comparatively new and rising technology, to phenotype avian embryo hearts in a model of fetal alcohol syndrome where a binge-like quantity of alcohol/ethanol was introduced at gastrulation.

RESULTS:
The rapid, consistent imaging protocols allowed for the immediate identification of cardiac anomalies, including ventricular septal defects and misaligned/missing vessels. Interventricular septum thicknesses and vessel diameters for three of the five outflow arteries were also significantly reduced. Outflow and atrioventricular valves were segmented using image processing software and had significantly reduced volumes compared to controls. This is the first study to our knowledge that...
has 3D reconstructed the late-stage cardiac valves in precise detail to examine their morphology and dimensions.

CONCLUSIONS:
We believe, therefore, that optical coherence tomography, with its ability to rapidly image and quantify tiny embryonic structures in high resolution, will serve as an excellent and cost-effective preliminary screening tool for developmental biologists working with a variety of experimental/disease models.

Read Full Article
Back to Table of Contents


143. Importance of genetics in fetal alcohol effects: null mutation of the nNOS gene worsens alcohol-induced cerebellar neuronal losses and behavioral deficits.
Bonthius DJ Jr, Winters Z, Karacay B, Bousquet SL, Bonthius DJ. (USA); daniel-bonthius@uiowa.edu

ABSTRACT
The cerebellum is a major target of alcohol-induced damage in the developing brain. However, the cerebella of some children are much more seriously affected than others by prenatal alcohol exposure. As a consequence of in utero alcohol exposure, some children have substantial reductions in cerebellar volume and corresponding neurodevelopmental problems, including microencephaly, ataxia, and balance deficits, while other children who were exposed to similar alcohol quantities are spared. One factor that likely plays a key role in determining the impact of alcohol on the fetal cerebellum is genetics. However, no specific gene variant has yet been identified that worsens cerebellar function as a consequence of developmental alcohol exposure. Previous studies have revealed that mice carrying a homozygous mutation of the gene for neuronal nitric oxide synthase (nNOS/-/- mice) have more severe acute alcohol-induced neuronal losses from the cerebellum than wild type mice. Therefore, the goals of this study were to determine whether alcohol induces more severe cerebellum-based behavioral deficits in nNOS/-/- mice than in wild type mice and to determine whether these worsened behavior deficits are associated with worsened cerebellar neuronal losses. nNOS/-/- mice and their wild type controls received alcohol (0.0, 2.2, or 4.4mg/g) daily over postnatal days 4-9. In adulthood, the mice underwent behavioral testing, followed by neuronal quantification. Alcohol caused dose-related deficits in rotarod and balance beam performance in both nNOS/-/- and wild type mice. However, the alcohol-induced behavioral deficits were substantially worse in the nNOS/-/- mice than in wild type. Likewise, alcohol exposure led to losses of Purkinje cells and cerebellar granule cells in mice of both genotypes, but the cell losses were more severe in the nNOS/-/- mice than in wild type. Behavioral performances were correlated with neuronal number in the nNOS/-/- mice, but not in wild type. Thus, homozygous mutation of the nNOS gene increases vulnerability to alcohol-induced cerebellar dysfunction and neuronal loss. nNOS is the first gene identified whose mutation worsens alcohol-induced cerebellar behavioral deficits.

Read Full Article
http://www.ncbi.nlm.nih.gov/pubmed/25511929
Back to Table of Contents


144. Effects of low-level alcohol use on cognitive interference: an fMRI study in young adults.
Hatchard T, Smith AM, Halchuk RE, Longo CA, Fried PA, Hogan MJ, Cameron I. (Canada)
ABSTRACT
Alcohol consumption is widely known to adversely affect human health. Its neuropathology is largely evident in the cerebellum and frontal lobes, particularly in the immature brains of adolescents and young adults. It may also have a long-lasting impact on executive functioning. The Ottawa Prenatal Prospective Study (OPPS) has followed participants over 20 years, from birth to young adulthood, and has collected data on potentially confounding lifestyle variables, such as prenatal drug exposure and current drug use. The present study investigated the neural activity of 29 young adults from the OPPS using fMRI. The main objective was to discover the impact of regular low-level alcohol consumption on the cognitive interference of these participants, as they performed a Counting Stroop task. Results indicated that, despite a lack of performance differences, young adults who use alcohol on a regular basis differ significantly from non-users with respect to their neural activity as they perform this task. Areas that were significantly more activated in users compared to non-users included the cerebellum, thalamus, fusiform gyrus, prefrontal cortex, and precuneus. The observed activity suggests a significant impact of early alcohol use on neurocognitive functioning despite relatively low levels of alcohol consumption.

Read Full Article
Back to Table of Contents

Lundsberg LS, Illuzzi JL, Belanger K, Triche EW, Bracken MB. (USA), michael.bracken@yale.edu

ABSTRACT
PURPOSE:
To estimate whether low-to-moderate prenatal alcohol exposure is associated with selected birth outcomes.

METHODS:
Low-to-moderate prenatal alcohol drinking and effects on low birthweight, preterm delivery, intrauterine growth restriction, and selected neonatal outcomes were evaluated among 4496 women and singleton infants. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multivariable logistic regression, controlling for confounding variables.

RESULTS:
Early pregnancy drinking was associated with reduced odds of low birthweight, OR, 0.66 (95% CI, 0.46-0.96) and birth length less than 10th percentile, OR, 0.74 (95% CI, 0.56-0.97). Drinking during the first 3 months showed lower odds for birth length and head circumference less than 10th percentile, OR, 0.56 (95% CI, 0.36-0.87) and OR, 0.69 (95% CI, 0.50-0.96), respectively. Third trimester drinking was associated with lower odds for low birthweight, OR, 0.56 (95% CI, 0.34-0.94) and preterm delivery, OR, 0.60 (95% CI, 0.42-0.87).

CONCLUSIONS:
Our results suggest low-to-moderate alcohol exposure during early and late gestation is not associated with increased risk of low birthweight, preterm delivery, intrauterine growth restriction, and most selected perinatal outcomes.

Read Full Article
Back to Table of Contents
Neonatal sensitization to ethanol-induced breathing disruptions as a function of late prenatal exposure to the drug in the rat: modulatory effects of ethanol's chemosensory cues.

Cullere M, Macchione AF, Haymal B, Paradelo M, Langer MD, Spear NE, Molina JC. (Argentina); jmolina@immf.uncor.edu

ABSTRACT

Preclinical and clinical studies have systematically demonstrated abrupt changes in fetal respiratory patterns when the unborn organism is exposed to the effects of maternal ethanol intoxication. In subprimates, chronic exposure to this drug during gestation and infancy results in marked alterations of the plasticity of the respiratory network. These alterations are manifested in terms of an early incapability to overcome deleterious effects of hypoxic events as well as in terms of sensitization to ethanol's depressant effects upon breathing patterns. It has also been demonstrated that near term rat fetuses process ethanol's chemosensory cues when the drug contaminates the amniotic fluid and that associative learning processes occur due to the temporal contiguity existing between these cues and different ethanol-related physiological effects. In the present study during the course of late gestation (gestational days 17-20), pregnant rats were intragastrically administered with either 0.0 or 2.0 g/kg ethanol. Seven-day-old pups derived of these dams were evaluated in terms of respiration rates (breaths/min) and apneas when subjected to different experimental conditions. These conditions were defined by postnatal exposure to the drug (intragastric administrations of either 0.0, 0.5, 1.0 or 2.0 g/kg ethanol), postadministration time of evaluation (5-10 or 30-35 min) and olfactory context at test (no explicit ambient odor or ethanol ambient odor). The results, obtained via whole body plethysmography, indicated that brief prenatal experience with the drug sensitized the organisms to ethanol's depressant effects particularly when employing the higher ethanol doses. In turn, presence of ethanol odor at test potentiated the above mentioned respiratory alterations. Prenatal treatment with ethanol was not found to alter pharmacokinetic profiles resulting from postnatal exposure to the drug or to affect different morphometric parameters related with lung development. These results indicate that even brief exposure to the drug during late gestation is sufficient to sensitize the organism to later disruptive effects of the drug upon breathing responsiveness. These deficits are potentiated through the re-exposure to the olfactory context perceived in utero which is known to be associated with ethanol's unconditioned effects. As a function of these observations it is possible to suggest a critical role of fetal sensory and learning capabilities in terms of modulating later ethanol-related breathing disruptions.

Read Full Article
Back to Table of Contents

Mental and Motor Development of Children with Preterm Birth and Children with Fetal Alcohol Syndrome.

Feldmann R, Girke N. (Germany)

ABSTRACT

OBJECTIVE:

Children with preterm birth (PTB), particularly if medical complications after birth are recorded, are at risk of developmental handicaps. More than half of the children with fetal alcohol syndrome (FAS) are born preterm.

METHODS:

Using the Bayley Scales of Infant Development - Second Edition, we assessed the mental (MDI) and psychomotor development (PDI) of children with PTB and children with FAS. PTB children without (PTB_c-, N=31) and with (PTB_c+, N=17) medical complications as well as children with
FAS (N=30; N=10 preterm, N=14 in term; N=6 not known) were tested at the age of 2 years (PTB: M=25 months, SD=3 months; FAS: M=27 months, SD=6 months).

RESULTS:
PTBc+ (MDI=85; PDI=80) as well as FAS (MDI=79; PDI=80) children show a poorer mental and motor development than PTBc- (MDI=99; PDI=92) children. FAS children with PTB show a significantly higher mental development (MDI=84) than FAS children born in term (MDI=75), while there are no differences concerning their motor development (PDI=79 in both groups).

DISCUSSION:
The results demonstrate that children with FAS are as developmental delayed as PTBc+children. PTB itself, although frequently occurring in FAS, seems not to exacerbate the mental or motor development deficits in children with FAS. Quite the contrary, developmental delay in FAS children seems to be positively moderated by PTB, as being born preterm is cutting short the noxious intrauterine alcohol exposition of the child.

148. Reversal of glucose intolerance in rat offspring exposed to ethanol before birth through reduction of nuclear skeletal muscle HDAC expression by the bile acid TUDCA.
Yao XH, Nguyen KH, Nyomba BL. (Canada)

ABSTRACT
Prenatal ethanol exposure causes cellular stress, insulin resistance, and glucose intolerance in adult offspring, with increased gluconeogenesis and reduced muscle glucose transporter-4 (glut4) expression. Impaired insulin activation of Akt and nuclear translocation of histone deacetylases (HDACs) in the liver partly explain increased gluconeogenesis. The mechanism for the reduced glut4 is unknown. Pregnant rats were gavaged with ethanol over the last week of gestation and adult female offspring were studied. Some ethanol-exposed offspring was treated with tauroursodeoxycholic acid (TUDCA) for 3 weeks. All these rats underwent intraperitoneal glucose tolerance and insulin tolerance tests. The expression of glut4, HDACs, and markers of endoplasmic reticulum (ER) unfolded protein response (XBP1, CHOP, ATF6) was examined in the gastrocnemius muscle fractions, and in C2C12 muscle cells cultured with ethanol, TUDCA, and HDAC inhibitors. Non-TUDCA-treated rats exposed to prenatal ethanol were insulin resistant and glucose intolerant with reduced muscle glut4 expression, increased ER marker expression, and increased nuclear HDACs, whereas TUDCA-treated rats had normal insulin sensitivity and glucose tolerance with normal glut4 expression, ER marker expression, and HDAC levels. In C2C12 cells, ethanol reduced glut4 expression, but increased ER markers. While TUDCA restored glut4 and ER markers to control levels and HDAC inhibition rescued glut4 expression, HDAC inhibition had no effect on ER markers. The increase in nuclear HDAC levels consequent to prenatal ethanol exposure reduces glut4 expression in adult rat offspring, and this HDAC effect is independent of ER unfolded protein response. HDAC inhibition by TUDCA restores glut4 expression, with improvement in insulin sensitivity and glucose tolerance.

149. Prenatal alcohol exposure alters response of kisspeptin-ir neurons to estradiol and progesterone in adult female rats.
ABSTRACT

BACKGROUND:
Prenatal alcohol exposure (PAE) has adverse effects on reproductive function and hypothalamic-pituitary-gonadal (HPG) activity. Kisspeptin neurons play a role in mediating feedback effects of estradiol (E2) and progesterone (P4) on the HPG axis. We hypothesized that PAE will have long-term effects on the response of kisspeptin neurons to E2 and P4.

METHODS:
Adult female rats (53 to 58 days) from prenatal ad libitum-fed control (C), pair-fed (PF), and alcohol-exposed (PAE) groups were subjected to Sham ovariectomy (OVX) or OVX without or with replacement with low or high physiological levels of E2 and P4, and terminated under basal conditions. E2 and P4 levels, and the response of kisspeptin-ir neurons in the arcuate (ARC) and anteroventral periventricular (AVPV) nuclei to these hormones, were measured. As the E2 signal is conveyed to kisspeptin neurons via estrogen receptor-α (ER-α), we investigated PAE effects on the number of kisspeptin-ir/ER-α-ir neurons. To determine whether PAE alters interactions between kisspeptin and gonadotropin-releasing hormone (GnRH) neurons, close contacts between kisspeptin-ir fibers and GnRH-ir cell bodies were examined.

RESULTS:
Our data present the novel finding that kisspeptin-ir neurons in the ARC of PAE females show differential responses to E2 and to the combined treatment with E2 and P4 compared with controls: (i) OVX increased the number of kisspeptin-ir neurons in C and PF, but not PAE females compared with their Sham counterparts; (ii) E2 replacement restored kisspeptin-ir cell numbers to Sham levels in C and PF females but caused a robust down-regulation of kisspeptin-ir neurons below Sham levels in PAE females; (iii) OVX and replacement with high physiological concentrations of E2 resulted in fewer kisspeptin-ir cells in PAE than C females; (iv) OVX and replacement with high levels of both E2 and P4 markedly decreased the number of kisspeptin-ir neurons, below levels observed following E2 alone, in PF and C females, but had no significant effect in PAE females.

CONCLUSIONS:
These data suggest that a possible mechanism underlying adverse effects of PAE on HPG function involves actions of alcohol on the kisspeptin system.

Read Full Article
Back to Table of Contents

Congenit Heart Dis. 2015 Jun 1. doi: 10.1111/chd.12271. [Epub ahead of print]

150. Maternal Alcohol Consumption before and during Pregnancy and the Risks of Congenital Heart Defects in Offspring: A Systematic Review and Meta-analysis.
Sun J, Chen X, Chen H, Ma Z, Zhou J. (China)

ABSTRACT

OBJECTIVE:
Epidemiologic studies have reported conflicting results regarding maternal alcohol consumption before and during pregnancy, and the risk of congenital heart defects (CHDs). However, a systematic review and meta-analysis of the association between maternal alcohol consumption and CHDs in offspring has not been conducted.

DESIGN:
We searched MEDLINE and EMBASE for articles catalogued between their inception and February 16, 2015; we identified relevant published studies that assessed the association between maternal alcohol consumption and CHD risk. Two authors independently assessed the
 eligibility of the retrieved articles and extracted data from them. Study-specific relative risk estimates were pooled by random-effects or fixed-effects models.

RESULTS:
From the 1527 references, a total of 19 case-control studies and four cohort studies were enrolled in this meta-analysis. The summary of 23 studies related to CHDs indicated an overall pooled relative risk of 1.13 (95% confidence interval: 0.96, 1.29) among mothers drinking before or during pregnancy. Statistically significant heterogeneity was detected (Q = 196.61, P < .001, I² = 88.8%) with no publication bias (Egger's test: P = .157). We conducted stratified and meta-regression analyses to identify the origin of the heterogeneity among studies.

CONCLUSION:
In summary, this meta-analysis provided no positive association between maternal alcohol consumption and risk of CHDs.

Read Full Article

Back to Table of Contents

151. FAS, FASD: Diagnosis and Myths
Barry C. Stanley (Canada)

ABSTRACT
The myth that fetal alcohol syndrome (FAS) is the most severe form of fetal alcohol spectrum disorder (FASD) causes confusion and erroneous conclusions. It is not just a matter of semantics. In a recent appeal case the expert witness for the crown stated that the appellant was not severely affected since he did not have the facial features. When such an erroneous statement is accepted as fact and incorporated into the legal system it becomes an obstruction in the pursuit of justice.

Read Full Article
http://www.jptcp.com/pubmed.php?articleId=510

Back to Table of Contents

152. Implementing staff-administered TACER-3 alcohol screening in an antenatal clinic
Lisa Chiodo, John Hannigan, Shobha Mehta, James Janisse, Virginia Delaney-Black, Deborah Walker, Robert Sokol

ABSTRACT
OBJECTIVE
TACER-3 is an adapted re-scoring of the T-ACE pregnancy alcohol screen. Our prior studies in a research setting showed that TACER-3 is more specific than T-ACE, better predicting risk drinking in pregnancy & alcohol-related neurobehavioral deficits in offspring. Though clinical use of the TACER-3 could result in better utilization of health care provider time by focusing effort on women drinking at fetal risk levels, surveys of ObGyns have shown repeatedly that few actually do formal screening, substantially under-identifying pregnancy risk drinking. Our purpose here was to investigate the feasibility & effectiveness of using the TACER-3 administered by antenatal office staff.
STUDY DESIGN

Current standard of care (SOC) alcohol screening by history was evaluated via chart review. Then, with endorsement of clinic managers, staff was trained in Fetal Alcohol Spectrum Disorders (FASD) and in use of the TACER-3, which was then implemented in the same clinic. Identification of risk drinking using SOC was compared to subsequent identification of risk drinking using TACER-3, as well as the original T-ACE.

RESULTS

Compared with SOC (5/365; 1.4%), TACER-3 was more likely to identify women as drinking at risk levels during pregnancy (41/448; 9.2% - $\chi^2 = 22.8, \ p<0.001$). In contrast, T-ACE identified 22.1% (99/448) of the women as risk drinkers, significantly more frequently than did the TACER-3 ($\chi^2 = 159.1, \ p<0.001$).

CONCLUSION

Implementing TACER-3 screening in an antenatal practice increased the rate of identifying women drinking at fetal risk levels during pregnancy above SOC screening by more than 6-fold and was more selective than the original T-ACE screen by reducing “false positives.” The implications are that training staff about FASD and implementation of the TACER-3 in clinical practice may allow for more efficient use of health care provider time in effectively identifying pregnant women most at risk for alcohol-related adverse fetal outcomes and most in need of intervention. Supported by a WSU Inphaase Grant.

Read Full Article
http://www.ajog.org/article/S0002-9378(14)01285-X/fulltext

Back to Table of Contents


153. Prenatal ethanol exposure alters ethanol-induced Fos immunoreactivity and dopaminergic activity in the mesocorticolimbic pathway of the adolescent brain.

Fabio MC, Vivas L, Pautassi RM. (Argentina); rpautassi@gmail.com

ABSTRACT

Prenatal ethanol exposure (PEE) promotes alcohol intake during adolescence, as shown in clinical and pre-clinical animal models. The mechanisms underlying this effect of prenatal ethanol exposure on postnatal ethanol intake remain, however, mostly unknown. Few studies assessed the effects of moderate doses of prenatal ethanol on spontaneous and ethanol induced brain activity on adolescence. This study measured, in adolescent (female) Wistar rats prenatally exposed to ethanol (0.0 or 2.0 g/kg/day, gestational days 17-20) or non-manipulated (NM group) throughout pregnancy, baseline and ethanol-induced cathecolaminergic activity (i.e., colocalization of c-Fos and tyrosine hydroxylase) in ventral tegmental area (VTA), and baseline and ethanol-induced Fos immunoreactivity (ir) in nucleus accumbens shell and core (AcbSh and AcbC, respectively) and prelimbic (PrL) and infralimbic (IL) prefrontal cortex. The rats were challenged with ethanol (dose: 0.0, 1.25, 2.5 or 3.25 g/kg, i.p.) at postnatal day 37. Rats exposed to vehicle prenatally (VE group) exhibited reduced baseline dopaminergic tone in VTA; an effect that was inhibited by prenatal ethanol exposure (PEE group). Dopaminergic activity in VTA after the postnatal ethanol challenge was greater in PEE than in VE or NM animals. Ethanol-induced Fos-ir at AcbSh was found after 1.25 g/kg and 2.5 g/kg ethanol, in VE and PEE rats, respectively. PEE did not alter ethanol-induced Fos-ir at IL but reduced ethanol-induced Fos-ir at PrL. These results suggest that prenatal ethanol exposure heightens dopaminergic activity in the VTA and alters the response of the mesocorticolimbic pathway to postnatal ethanol exposure. These effects may underlie the enhanced vulnerability to develop alcohol use disorders of adolescents with a history of in-utero ethanol exposure.
154. Impaired arousal in rat pups with prenatal alcohol exposure is modulated by GABAergic mechanisms.

Sirieix CM, Tobia CM, Schneider RW, Darnall RA. (USA); chrystelle.sirieix@gmail.com

**ABSTRACT**

Prenatal alcohol exposure (PAE) increases the risk for The Sudden Infant Death Syndrome (SIDS) in human infants. In rat pups, the arousal response to hypoxia is modulated by medullary raphe GABAergic mechanisms. We hypothesized that arousal to hypoxia is impaired by PAE, and is associated with an increase in medullary GABA and enhanced GABAergic activity. Pregnant dams received an ethanol liquid diet (ETOH), an iso-caloric pair fed diet (PF) or a standard chow diet (CHOW). We first measured the time to arousal (latency), during four episodes of hypoxia in P5, P15, and P21 CHOW, PF, and ETOH pups. We also measured brainstem GABA concentration in the same groups of pups. Finally, we injected artificial cerebrospinal fluid (aCSF), nipecotic acid (NIP) or gabazine into the medullary raphe of P15 and P21 pups receiving the three diets. For statistical analysis, the PF and CHOW groups were combined into a single CONTROL group. Our main finding was that compared to CONTROL, arousal latency to hypoxia is increased in ETOH pups at P15 and P21, and the concentration of brainstem GABA is elevated at P21. NIP administration in CONTROL pups led to arousal latencies similar in magnitude to those in ETOH pups after aCSF injection. NIP injected ETOH pups had no further increases in arousal latency. We conclude that PAE impairs arousal latency and this is mediated or modulated by medullary GABAergic mechanisms.

Read Full Article
Back to Table of Contents


155. Ethanol-related alterations in gene expression patterns in the developing murine hippocampus.

Mandal C, Park KS, Jung KH, Chai YG. (Republic of Korea); ygchai@hanyang.ac.kr, khjung2@gmail.com

**ABSTRACT**

It is well known that consuming alcohol prior to and during pregnancy can cause harm to the developing fetus. Fetal alcohol spectrum disorder is a term commonly used to describe a range of disabilities that may arise from prenatal alcohol exposure such as fetal alcohol syndrome, partial fetalalcohol syndrome, alcohol-related neurodevelopmental disorders, and alcohol-related birth defects. Here, we report that maternal binge alcoholconsumption alters several important genes that are involved in nervous system development in the mouse hippocampus at embryonic day 18. Microarray analysis revealed that Nova1, Ntng1, Gal, Neurog2, Neurod2, and Fezf2 gene expressions are altered in the fetal hippocampus. Pathway analysis also revealed the association of the calcium signaling pathway in addition to other pathways with the differentially expressed genes during early brain development. Alteration of such important genes and dynamics of the signaling pathways may cause neurodevelopmental disorders. Our findings offer insight into the molecular mechanism involved in neurodevelopmental disorders associated with alcohol-related defects.

Read Full Article
Back to Table of Contents
156. Costs of Fetal Alcohol Spectrum Disorder in the Canadian Criminal Justice System.  
Thanh NX, Jonsson E. (Canada)

ABSTRACT
We reviewed literature to estimate the costs of Fetal Alcohol Spectrum Disorder (FASD) in the Canadian Criminal Justice System (CJS), and to update the total costs of FASD in Canada. The results suggest FASD is costlier than previous estimates. The costs of FASD associated with the CJS are estimated at $3.9 billion a year, with $1.2 billion for police, $0.4 billion for court, $0.5 billion for correctional services, $1.6 billion for victims, and $0.2 billion for third-party. The updated total costs of FASD in Canada are $9.7 billion a year, of which CJS accounts for 40%, healthcare 21%, education 17%, social services 13%, and others 9%.

Read Full Article
Back to Table of Contents

157. Effect of Depression on Risky Drinking and Response to a Screening, Brief Intervention, and Referral to Treatment Intervention.  
Montag AC, Brodine SK, Alcaraz JE, Clapp JD, Allison MA, Calac DJ, Hull AD, Gorman JR, Jones KL, Chambers CD. (USA)

ABSTRACT
We assessed alcohol consumption and depression in 234 American Indian/Alaska Native women (aged 18-45 years) in Southern California. Women were randomized to intervention or assessment alone and followed for 6 months (2011-2013). Depression was associated with risk factors for alcohol-exposed pregnancy (AEP). Both treatment groups reduced drinking (P < .001). Depressed, but not nondepressed, women reduced drinking in response to SBIRT above the reduction in response to assessment alone. Screening for depression may assist in allocating women to specific AEP prevention interventions.

Read Full Article
Back to Table of Contents

158. Exposure to tobacco, alcohol and drugs of abuse during pregnancy. A study of prevalence among pregnant women in Malaga (Spain).  
[Article in English, Spanish]
Blasco-Alonso M, González-Mesa E, Gálvez Montes M, Lozano Bravo I, Merino Galdón F, Cuenca Campos F, Marín Schiaffino G, Pérez Torres S, Herrera Peral J, Bellido Estévez I. (Spain); egonzalezmesa@gmail.com

ABSTRACT
The prevalence of substance abuse in women who become pregnant is similar to that of the general population, resulting in a high fetal exposure rate during the most vulnerable period regarding neurodevelopment and organogenesis. The present study was intended to assess the level of prenatal exposure to tobacco, alcohol or illicit drugs in the city of Málaga (Spain). It was designed as a cross-sectional study, and based on the anonymous self-reports of participants. A total of 451
pregnant women were recruited in the first, second or third trimester. The prevalence in each of the quarters respectively was 21.2%, 18.5% and 13.3% for smoking, 40.7%, 23.1% and 17.1% for alcohol and 4.8%, 1.9% and 1.2% for cannabis. We also found that a higher educational level was associated with a lower consumption of tobacco (RR 0.659 [0.537-0.810] p<0.0001) and greater exposure to alcohol (RR 1.87 [1.30-2.69] p<0.0007). These results, particularly in regard to alcohol intake, are sufficiently alarming to alert obstetric care providers about the need to implement preventive measures.

Read Full Article
Back to Table of Contents

159. Alcohol use, smoking and their co-occurrence during pregnancy among Canadian women, 2003 to 2011/12.
Lange S, Probst C, Quere M, Rehm J, Popova S. (Canada, France, Germany); lana.popova@camh.ca.

ABSTRACT
INTRODUCTION:
The co-occurrence of alcohol use and smoking during pregnancy has been shown to have a negative synergistic effect on fetal and perinatal risks. The objectives were to: 1) obtain an estimate of the prevalence of smoking during pregnancy in Canada by province and territory from 2003 to 2011/12; 2) determine if the prevalence of smoking during pregnancy has increased or decreased over time; 3) investigate whether smoking status is differentially associated with alcohol use during pregnancy; and 4) examine the risk factors predictive of alcohol use only, smoking only, and the co-occurrence of alcohol use and smoking during pregnancy.

METHODS:
Secondary data analysis was conducted using five cycles of the Canadian Community Health Survey (CCHS; 2003, 2005, 2007/08, 2009/10 and 2011/12). The prevalence of smoking during pregnancy, and 95% confidence interval (CI) was calculated by province and territory and by year. The likelihood ratio test was used to determine if the prevalence of smoking during pregnancy has increased or decreased over time. The relationship between smoking status and alcohol use during pregnancy was explored using a quasi-Poisson regression model. A multinomial logistic regression model was utilized to determine which factors were predictive of alcohol use only, smoking only, and the co-occurrence of alcohol use and smoking during pregnancy.

RESULTS:
In Canada, between 2003 and 2011/12, the weighted pooled prevalence of smoking during pregnancy was 14.3% (95% CI: 13.6%-15.0%). Women who smoked daily during pregnancy, occasionally during pregnancy, or had a lifetime history of smoking (but did not smoke while pregnant) were 2.54 (95% CI: 2.11-3.06, P<0.0001), 2.71 (95% CI: 2.25-3.27, P<0.0001), and 2.09 (95% CI: 1.85-2.37, P<0.0001), respectively, times more likely to have consumed alcohol during pregnancy, compared to pregnant women who were lifetime non-smokers when controlling for age, household income, ethnicity and CCHS cycle. Risk factors that predicted alcohol use only, smoking only, and the co-occurrence of alcohol use and smoking during pregnancy differed.

CONCLUSION:
It is apparent that smoking in any capacity, whether during pregnancy or not, increases the likelihood that a woman consumed alcohol while pregnant. Ascertain smoking status among pregnant women and women of childbearing age could be a useful screening method for identifying those at-risk of consuming alcohol during pregnancy, and vice versa.
160. The Knowledge of Rehabilitation Professionals Concerning Fetal Alcohol Spectrum Disorders.
Birch SM, Carpenter HA, Marsh AM, McClung KA, Doll JD. (USA)

ABSTRACT
The purpose of this study was to explore rehabilitation professionals' knowledge regarding signs and symptoms, prevention, and intervention of fetal alcohol spectrum disorders (FASD). Participants were 111 rehabilitation practitioners (e.g., occupational therapy, physical therapy, and speech-language pathology practitioners) recruited through email using a quantitative online survey design with purposive, snowball sampling. Results showed the majority of participants' demonstrated accurate knowledge of the signs and symptoms of FASD. Since professionals who received formal education on FASD reported significantly higher feelings of preparedness to identify children with FASD and manage/coordinate intervention plans, this study suggests rehabilitation professionals may be better prepared to treat individuals with FASD if they participate in formal training.

McCoy SW, Jirikowic T, Price R, Ciol MA, Hsu LY, Dellon B, Kartin D. (USA)

ABSTRACT
BACKGROUND:
Diminished sensory adaptation has been associated with poor balance control for children with fetal alcohol spectrum disorders (FASD). We developed a virtual reality system, Sensorimotor Training to Affect Balance, Engagement and Learning (STABEL), to train sensory control for balance.

OBJECTIVES:
We examined the STABEL system with children with FASD and children with typical development (TD). Our purposes were to 1) determine the feasibility of the STABEL system and 2) explore the immediate effects of STABEL on sensory attention and postural control.

DESIGN:
Observational study.

METHODS:
Eleven children with FASD and 11 with TD, 8-16 years, completed 30 minutes of STABEL training. Children answered questions about their experience using STABEL. Sensory attention and postural control were measured pre- and post-STABEL training with the Multimodal Balance Entrainment Response system and compared using repeated measures ANOVA.
RESULTS:
All children engaged in game play and tolerated controlled sensory input during the STABEL protocol. Immediate effects post-STABEL training in both groups were increased postural sway velocity (P < 0.05) and some changes in entrainment gain (P < 0.10). Children with FASD showed higher entrainment gain to vestibular stimuli (P < 0.10). There were no significant changes in sensory attention fractions.

LIMITATIONS:
The small sample size, dose of STABEL, and exploratory statistical analyses are study limitations, but findings warrant larger systematic study to examine therapeutic effects.

CONCLUSIONS:
Children completed the training protocol demonstrating the feasibility of the STABEL system. Differences in postural sway velocity post STABEL may have been affected by fatigue, requiring further investigation. Limited immediate effects suggest more practice is needed to affect sensory attention; however, entrainment gain changes suggest the STABEL provoked vestibular responses during balance practice.

Read Full Article
Back to Table of Contents

162. Effects of Developmental Alcohol Exposure on Potentiation and Depression of Visual Cortex Responses.
Lantz CL, Sipe GO, Wong EL, Majewska AK, Medina AE. (USA)

ABSTRACT
BACKGROUND:
Neuronal plasticity deficits are thought to underlie abnormal neurodevelopment in fetal alcohol spectrum disorders and in animal models of this condition. Previously, we found that alcohol exposure during a period that is similar to the last months of gestation in humans disrupts ocular dominance plasticity (ODP), as measured in superficial cortical layers. We hypothesize that exposure to alcohol can differentially affect the potentiation and depression of responses that are necessary for activity-dependent sprouting and pruning of neuronal networks. ODP is an established paradigm that allows the assessment of activity-dependent depression and potentiation of responses in vivo.

METHODS:
Mouse pups were exposed to 3.6 to 5 g/kg of ethanol in saline daily or every other day between postnatal days 4 and 9. Visual cortex plasticity was then assessed during the critical period for ODP using 2 techniques that separately record in layers 4 (visually evoked potentials [VEPs]) and 2/3 (optical imaging of intrinsic signals [OI]).

RESULTS:
We discovered a layer-specific effect of early alcohol exposure. Recording of VEPs from layer 4 showed that while the potentiation component of ODP was disrupted in animals treated with alcohol when compared with saline controls, the depression component of ODP (Dc-ODP) was unaltered. In contrast, OI from layers 2/3 showed that Dc-ODP was markedly disrupted in alcohol-treated animals when compared with controls.

CONCLUSIONS:
Combined with our previous work, these findings strongly suggest that developmental alcohol exposure has a distinct and layer-specific effect on the potentiation and depression of cortical responses after monocular deprivation.

Read Full Article
Back to Table of Contents

Behav Brain Res. 2015 Jun 18;292:102-108. doi: 10.1016/j.bbr.2015.05.060. [Epub ahead of print]

Fernandes Y, Rampersad M, Gerlai R. (Canada); robert_gerlai@yahoo.com

ABSTRACT
Zebrafish naturally form social groups called shoals. Previously, we have shown that submerging zebrafish eggs into low concentrations of alcohol (0.00, 0.25, 0.50, 0.75 and 1.00 vol/vol% external bath concentration) during development (24h post-fertilization) for two hours resulted in impaired shoaling response in seven month old young adult zebrafish. Here we investigate whether this embryonic alcohol exposure induced behavioural deficit persists to older age. Zebrafish embryos were exposed either to fresh system water (control) or to 1% alcohol for two hours, 24h after fertilization, and were raised in a high-density tank system. Social behaviour was tested by presenting the experimental fish with a computer animated group of zebrafish images, while automated tracking software measured their behaviour. Control fish were found to respond strongly to animated conspecific images by reducing their distance and remaining close to the images during image presentation, embryonic alcohol treated fish did not. Our results suggest that the impaired shoaling response of the alcohol exposed fish was not due to altered motor function or visual perception, but likely to a central nervous system alteration affecting social behaviour itself. We found the effects of embryonic alcohol exposure on social behaviour not to diminish with age, a result that demonstrates the deleterious and potentially life-long consequences of exposure to even small amount of alcohol during embryonic development in vertebrates.

Read Full Article
Back to Table of Contents

Cereb Cortex. 2015 Jun 17. pii: bhv131. [Epub ahead of print]

164. Prenatal Alcohol Exposure is Associated with Regionally Thinner Cortex During the Preadolescent Period.
Robertson FC, Narr KL, Molteno CD, Jacobson JL, Jacobson SW, Meintjes EM. (USA, South Africa)

ABSTRACT
Children with fetal alcohol spectrum disorders (FASD) may exhibit craniofacial dysmorphology, neurobehavioral deficits, and reduced brain volume. Studies of cortical thickness in FASD have yielded contradictory findings, with 3 reporting thicker cerebral cortex in frontal and temporal brain regions and 2 showing thinner cortex across multiple regions. All 5 studies included subjects spanning a broad age range, and none have examined continuous measures of prenatal alcohol exposure. We investigated the relation of extent of in utero alcohol exposure to cortical thickness in 78 preadolescent children with FASD and controls within a narrow age range. A whole-brain analysis using FreeSurfer revealed no significant clusters where cortical thickness differed by FASD diagnostic group. However, alcohol dose/occasion during pregnancy was inversely related to cortical thickness in 3 regions-right cuneus/pericalcarine/superior parietal lobe, fusiform/lingual gyrus, and supramarginal/postcentral gyrus. The effect of prenatal alcohol exposure on IQ was mediated by cortical thickness in the right occipitotemporal region. It is noteworthy that a
continuous measure of maternal alcohol consumption during pregnancy was more sensitive than FASD diagnosis and that the effect on cortical thickness was most evident in relation to a measure of maternal binge drinking.

Read Full Article
Back to Table of Contents

Cerebellum. 2015 Jun 18. [Epub ahead of print]

165. Choline Ameliorates Deficits in Balance Caused by Acute Neonatal Ethanol Exposure.
Bearer CF, Wellmann KA, Tang N, He M, Mooney SM. (USA)

ABSTRACT
Fetal alcohol spectrum disorder (FASD) is estimated to occur in 1 % of all live births. The developing cerebellum is vulnerable to the toxic effects of alcohol. People with FASD have cerebellar hypoplasia and developmental deficits associated with cerebellar injury. Choline is an essential nutrient, but many diets in the USA are choline deficient. In rats, choline given with or following alcohol exposure reduces many alcohol-induced neurobehavioral deficits but not those associated with cerebellar function. Our objective was to determine if choline supplementation prior to alcohol exposure would ameliorate the impact of ethanol on a cerebellar-associated behavioral test in mice. Pregnant C57Bl6/J mice were maintained on a choline-deficient diet from embryonic day 4.5. On postnatal day 1 (P1), pups were assigned to one of eight treatment groups: choline (C) or saline (S) pre-treatment from P1 to P5, ethanol (6 g/kg) or Intralipid® on P5, C and or S post-treatment from P6 to P20. On P30, balance and coordination were tested using the dowel crossing test. Overall, there was a significant effect of treatment and females crossed longer distances than males. Ethanol exposure significantly reduced the total distance crossed. Choline pre-treatment increased the distance crossed by males, and both pre- and post-treatment with choline significantly increased total distance crossed for females and males. There was no effect of choline on Intralipid®-exposed animals. This is the first study to show that choline ameliorates ethanol-induced effects on balance and coordination when given before ethanol exposure. Choline fortification of common foodstuffs may reduce the effects of alcohol.

Read Full Article
Back to Table of Contents


166. Embryonic alcohol exposure: Towards the development of a zebrafish model of fetal alcohol spectrum disorders.
Gerlai R. (Canada)

ABSTRACT
Fetal alcohol spectrum disorder (FASD) is a devastating disease of the brain caused by exposure to alcohol during prenatal development. Its prevalence exceeds 1%. The majority of FASD cases represent the milder forms of the disease which often remain undiagnosed, and even when diagnosed treatment options for the patient are limited due to lack of information about the mechanisms that underlie the disease. The zebrafish has been proposed as a model organism for exploring the mechanisms of FASD. Our laboratory has been studying the effects of low doses of alcohol during embryonic development in the zebrafish. This review discusses the methods of alcohol exposure, its effects on behavioral performance including social behavior and learning, and the potential underlying biological mechanisms in zebrafish. It is based upon a recent keynote address delivered by the author, and it focuses on findings obtained mainly in his own laboratory. It paints a promising future of this small vertebrate in FASD research.
167. *Embryonic catalase protects against ethanol embryopathies in acatalasemic mice and transgenic human catalase-expressing mice in embryo culture.*
Miller-Pinsler L, Wells PG. (Canada); pg.wells@utoronto.ca

**ABSTRACT**

Reactive oxygen species (ROS) have been implicated in the mechanism of ethanol (EtOH) teratogenicity, but the protective role of the embryonic antioxidative enzyme catalase is unclear, as embryonic activity is only about 5% of maternal levels. We addressed this question in a whole embryo culture model. C57BL/6 mouse embryos expressing human catalase (hCat) or their wild-type (C57BL/6 WT) controls, and C3Ga.Cg-Catb/J catalase-deficient, acatalasemic (aCat) mouse embryos or their wild-type C3HeB/FeJ (C3H WT) controls, were explanted on gestational day (GD) 9 (plug=GD 1), exposed for 24hr to 2 or 4mg/mL EtOH or vehicle, and evaluated for functional and morphological changes. hCat and C57BL/6 WT vehicle-exposed embryos developed normally, while EtOH was embryopathic in C57BL/6 WT embryos, evidenced by decreases in anterior neuropore closure, somites developed, turning and head length, whereas hCat embryos were protected (p<0.001). Maternal pretreatment of C57BL/6 WT dams with 50 kU/kg PEG-catalase (PEG-cat) 8hr prior to embryo culture, which increases embryonic catalase activity, blocked all EtOH embryopathies (p<0.001). Vehicle-exposed aCat mouse embryos had lower yolk sac diameters compared to WT controls, suggesting endogenous ROS are embryopathic. EtOH was more embryopathic in aCat embryos than WT controls, evidenced by reduced head length and somite development (p<0.01), and trends for reduced anterior neuropore closure, turning and crown-rump length. Maternal pretreatment of aCat dams with PEG-Cat blocked all EtOH embryopathies (p<0.05). These data suggest that embryonic catalase is a determinant of risk for EtOH embryopathies.

Read Full Article

168. *Antenatal alcohol exposure: An East Anglian study of midwives' knowledge and practice*  
Anne Marie Winstone & Christopher Verity (UK)

**ABSTRACT**

Objective: To study midwives’ knowledge, practice and opinions regarding advice about fetal alcohol syndrome (FAS), fetal alcohol spectrum disorders (FASDs) and alcohol intake in pregnancy. Design: A postal questionnaire was sent to 1862 midwives employed in 13 NHS Trusts in East Anglia, incorporating city and rural areas. Results: The authors received responses from 33.5% of the midwives contacted (n=624), of which 98% stated that alcohol abstinence in pregnancy would be their preferred advice, and 38% had seen an infant with FAS. Less than 2% indicated that they were ‘very prepared’ to deal with the subject. Only 10% identified all four classic features of FAS. Conclusions: More than a third of midwives had seen an infant with FAS. The advice given to...
pregnant mothers by participants varied. The midwives stated that they would like more information and support. Implications for practice: Expansion of midwives’ knowledge should improve the quality of antenatal advice, leading to better prevention, intervention and recognition of FASD in children.
A. Fetal Alcohol Spectrum Disorders (FASD) and Confabulation

A REVIEW FOR CRIMINAL JUSTICE PROFESSIONALS

Jerrod Brown, MA, MS, MS, MS, Pamela Oberoi MA, Jeffrey Long-McGie, MA, MBA, Judge Anthony (Tony) Wartnik, BA, JD, Erv Winkauf, MA, Sarah Herrick, MA, LP, LPCC, CCFC

Introduction

Confabulation is a commonly observed deficit in individuals with FASD. Simply, the act can be defined as the unintentional communication of falsehoods, incomplete information, and the absence of facts with no intent to deceive.

Confabulation among those with FASD may lead to a host of criminal justice consequences (e.g., false confessions and testimony, suggestibility, wrongful conviction, and subsequent imprisonment). FASD-related criminal justice consequences may also result in diminished comprehension of Miranda rights compromised ability to understand the filed criminal charges, and decreased understanding of the trial process…

Criminal Justice System

Criminal justice professionals are likely to come in contact with individuals with FASD on a regular basis. This may be partially related to deficits in adaptive behavior and executive functioning that are unrelated to IQ. The exact number of individuals with FASD currently in the criminal justice system is unknown; however, it is clear that FASD poses a significant problem for the criminal justice system. Prevalence rates in correctional settings have been reported to range from 10% to as high as 24% in two separate studies. A review of Canadian data found that those with FASD were 19 times more likely to be incarcerated compared to non-FASD-impacted individuals. Another study in the United States found that 60% of the participants with FASD over the age of 12 had been involved with the criminal justice system. Researchers from another study found that this population was 40 times more likely to be involved with the juvenile justice system.

Understanding crucial components of the legal process can be challenging for those with FASD. Deficits associated with a diagnosis of FASD may impact the ability for someone with this condition to understand their Miranda rights, interrogative procedures, and an overall comprehension of legal proceedings. FASD-associated deficits may also contribute to confabulation during various portions of the legal process. Criminal justice professionals should be aware that when interviewing someone with FASD they may unknowingly provide inaccurate information and contradictory statements.

Executive Functioning, Memory, and Social Skill Deficits

Executive functioning deficits are frequently observed in persons with FASD. Executive functioning deficits can have devastating effects on the individual and their ability to comprehend or communicate effectively. These deficits may also contribute to an increase in confabulation. Prenatal alcohol exposure has been associated with widespread neuropsychological deficits, which may amplify involvement in the criminal justice system. Such deficits can contribute to increased vulnerability, victimization, and subsequent legal involvement. FASD-related deficits can also impact daily functioning, general intelligence, memory, language, attention, learning, visuospatial abilities, fine and gross motor skills, and social and adaptive functioning. Impairments in verbal and nonverbal learning as well as memory, and social skill deficits have also been reported in FASD-
affected individuals. Diminished intellectual capacity is another common neurocognitive finding in individuals with FASD.

Confabulation

Confabulation is one of the many issues that can arise as a result of damage through prenatal alcohol exposure. Confabulation is not the same as lying. Confabulation can result in a wide range of errors in memory, including distortions, false realities of events, unintentional embellishments and elaborations of memory, and paraphrasing of existing memories. Confabulation among individuals with FASD can create complex legal issues for the criminal justice system. Unfortunately, professionals are rarely aware of the nature of confabulation and the factors contributing to this secondary consequence of FASD. Those with FASD who are suspects of a crime can be highly vulnerable to wrongful conviction and incarceration. Additionally, individuals with FASD who are witnesses to a crime may incorrectly report details of the event. Criminal justice professionals should be aware of the possible presence of confabulation and the consequences that may follow for individuals with FASD involved in the justice system.

Conclusion

FASD-related consequences may contribute to a host of adverse outcomes associated with the criminal justice system. Compared to non-FASD-impacted persons, those with FASD are more likely to confabulate, lack adequate understanding of Miranda and constitutional rights, and demonstrate impairments in the ability to understand the trial process. The presence of confabulation may be an indicator of a profound cognitive impairment. Criminal justice professionals should be aware that when interviewing someone with FASD, they may unknowingly provide inaccurate information and contradictory statements. As such, confabulation may greatly impact legal decisions and outcomes. Well-intentioned professionals may inadvertently not recognize the signs of confabulation. Confabulation can lead to the acknowledgement of a crime that was not committed. Recognition and knowledge of confabulation during the investigative process may prevent the potential for wrongful arrest, conviction, and subsequent incarceration of an innocent individual.

Read Full Article


B. Fathers drinking: Also responsible for fetal disorders?

Source: Taylor and Francis

14th February 2015

Maternal exposure to alcohol in-utero is a known risk and cause of Fetal Alcohol Syndrome. FAS children suffer significant problems such as retarded intellect, stunted growth and nervous system abnormalities, social problems and isolation. Until now Fathers have not had a causal link to such disabilities. Ground breaking new research has been revealed which shows Dads may have more accountability.

Published in Animal Cells and Systems, researchers studied male mice exposed to varying concentrations of alcohol and one control group exposed only to saline. After exposure the mice were mated and resulting fetuses examined. The findings revealed previously unknown and riveting evidence that paternal alcohol consumption can directly affect fetal development.
A number of fetuses sired by males exposed to alcohol suffered abnormal organ development and or brain development. Those in the saline group were normal. So, can developmental abnormalities be predetermined at fertilization? This research proves so. The authors believe alcohol consumption affects genes in sperm which are responsible for normal fetal development.

Until now fathers' lifestyle choices have not seen any repercussion on their unborn children. This ground-breaking research provides the first definitive evidence that fathers' drinking habits pre-conception can cause significant fetal abnormalities.

**Story Source:** Reprinted from materials provided by Taylor & Francis.


---

**C. High Rates of Missed Diagnoses of Fetal Alcohol Syndrome**

Health Day News

12th January, 2015

**Among youth, the rate of missed diagnosis or misdiagnosis of fetal alcohol spectrum disorders is 86.5 percent, according to a study published online Jan. 12 in Pediatrics.**

MONDAY, Jan. 12, 2015 (HealthDay News) -- Among youth, the rate of missed diagnosis or misdiagnosis of fetal alcohol spectrum disorders is 86.5 percent, according to a study published online Jan. 12 in Pediatrics.

Ira J. Chasnoff, M.D., from the Children's Research Triangle in Chicago, and colleagues collected data from a sample of 547 children among a population of foster and adopted youth who underwent a comprehensive multidisciplinary diagnostic evaluation. Children were diagnosed with fetal alcohol syndrome, partial fetal alcohol syndrome, alcohol-related neurodevelopmental disorder, or alcohol-related birth defects using current diagnostic criteria.

The researchers found that 125 of the 156 children and adolescents who met criteria for a diagnosis within the fetal alcohol spectrum had never been diagnosed as affected by prenatal alcohol exposure (missed diagnosis rate, 80.1 percent). Of the 31 children who had been recognized as affected by prenatal alcohol exposure before referral, 10 diagnoses were changed within the spectrum (misdiagnosis rate, 6.4 percent). The diagnoses of the remaining 21 children stayed the same. Significant changes were seen in the rate of mental health diagnoses; in a considerable number of children with fetal alcohol spectrum disorders, objective signs of neurocognitive damage (learning disorders, communication disorders, and intellectual disability) were not recognized.

"Within this clinical sample, 86.5 percent of youth with fetal alcohol spectrum disorders had never been previously diagnosed or had been misdiagnosed," the authors write. "These high rates of missed diagnoses and misdiagnosis have significant implications for intervention and therapeutic services."
Fetal alcohol syndrome (FAS) is a serious birth defect and developmental disorder caused by in utero exposure to alcohol (1). Assessment of the public health burden of FAS through surveillance has proven difficult; there is wide variation in reported prevalence depending on the study population and surveillance method. Generally, records-based birth prevalence studies report estimates of 0.2–1.5 per 1,000 live births (2), whereas studies that use in-person, expert assessment of school-aged children in a community report estimates of 6–9 per 1,000 population (3). The Fetal Alcohol Syndrome Surveillance Network II addressed some of the challenges in records-based ascertainment by assessing a period prevalence of FAS among children aged 7–9 years in Arizona, Colorado, and New York (4). The prevalence across sites ranged from 0.3 to 0.8 per 1,000 children. Prevalence of FAS was highest among American Indian/Alaska Native children and lowest among Hispanic children. These estimates continue to be much lower than those obtained from studies using in-person, expert assessment. Factors that might contribute to this discrepancy include 1) inadequate recognition of the physical and behavioral characteristics of FAS by clinical care providers; 2) insufficient documentation of those characteristics in the medical record; and 3) failure to consider prenatal alcohol exposure with diagnoses of behavioral and learning problems. Addressing these factors through training of medical and allied health providers can lead to practice changes, ultimately increasing recognition and documentation of the characteristics of FAS.

In 2009, CDC funded three sites, Arizona (statewide), Colorado (Denver-Boulder Consolidated Metropolitan Statistical Area), and New York (nine western counties), to conduct population-based surveillance of FAS in children aged 7–9 years who resided within the catchment areas in 2010. The surveillance methodology used by the sites is described in detail elsewhere (4). Sites used the standardized, multiple-source methodology developed by the Fetal Alcohol Syndrome Surveillance Network (2) that relied on passive reporting and active review of records from various sources to identify children with suspected FAS. Data from sources such as genetic and developmental clinics, hospital discharge files, Medicaid claims, health maintenance organization records, and the juvenile justice system were used for case finding.

A surveillance case definition (Table 1) was developed based on the 1996 Institute of Medicine report on FAS (1) and refined to reflect the older ages of the children in this cohort. Documentation of the features characteristic of FAS formed the basis of the case definition: facial dysmorphology, central nervous system (CNS) abnormalities, and growth deficiency. Maternal alcohol use during pregnancy was abstracted when available, but because of difficulty in obtaining reliable and valid documentation of this information, it was not required to meet the surveillance case definition.
confirmed case of FAS had documentation of facial features, CNS abnormalities, and growth deficiency; a probable case of FAS had documentation of facial features and either CNS abnormalities or growth deficiency (Table 1). Confirmed and probable cases were combined to estimate the prevalence of FAS. The denominator was the total number of children aged 7–9 years who resided in the catchment areas based on 2010 census estimates (5). Child’s race/ethnicity was reported if available; if the child’s race/ethnicity was missing, the race/ethnicity of the birth mother was used. Hispanic ethnicity was given priority over race, consistent with CDC’s National Center for Health Statistics guidelines.

The overall prevalence of FAS was 0.3 (95% confidence interval [CI] = 0.3–0.4) per 1,000 children aged 7–9 years; the site specific prevalence was 0.3 (CI = 0.2–0.3) in Arizona, 0.3 (CI = 0.2–0.4) in Colorado, and 0.8 (CI = 0.6–1.0) in New York (Table 2). Prevalence of FAS was highest among American Indian/Alaska Native children (2.0 [CI = 1.4–2.8] per 1,000 children aged 7–9 years) and lowest among Hispanic children (0.2 [CI = 0.1–0.2]). There were no differences in the prevalence of FAS by child’s age or sex.

Discussion

Despite the older age cohort and focus on a period prevalence, the prevalence estimates obtained from the Fetal Alcohol Syndrome Surveillance Network II are similar to previously reported birth prevalence estimates using records-based methodology and much lower than those estimated by in-person, expert assessment of children (3). Factors that might contribute to this discrepancy include 1) inadequate recognition of the physical and behavioral characteristics of FAS by clinical care providers; 2) insufficient documentation of those characteristics in the medical record and; 3) failure to consider prenatal alcohol exposure with diagnoses of behavioral and learning problems.

That these factors might contribute to the discrepancy is supported by the findings of a survey of pediatricians published in 2006 in which more than two-thirds of respondents reported a lack of training as the primary reason for not making a FAS diagnosis (6). More than half of respondents indicated that they had no formal training on the recognition, diagnosis, or treatment of FAS, and two-thirds thought this diagnosis would stigmatize the family and child (6). The lack of training has a cascading effect: clinicians do not recognize and document physical and behavioral characteristics that might lead to a more complete clinical evaluation or that would serve as a trigger for a records-based surveillance system to identify the child as potentially having FAS. Further, maternal prenatal records are not routinely linked to a child’s birth or neonatal record at the hospital, meaning that prenatal alcohol exposure, if documented in the maternal record, is not known to pediatric clinicians when interpreting physical or behavioral characteristics of the child. Finally, some clinicians are hesitant to consider possible prenatal alcohol exposure in the diagnosis of behavioral and learning problems because services or interventions specific to FAS are not available in their community or clinicians are unaware of such services in their community (6).

In 2014, CDC funded six Fetal Alcohol Spectrum Disorders (FASD) Practice and Implementation Centers.* These centers are designed to promote practice change among providers in the areas of FASD prevention, identification, and treatment. Two of the six centers will focus on pediatricians and are partnering with the American Academy of Pediatrics. Focused development of practice guidelines for pediatric clinicians through these Practice and Implementation Centers along with the broad-based dissemination capabilities of the American Academy of Pediatrics can improve identification, documentation, and clinical management of children with FAS, thereby strengthening the infrastructure needed for FAS records-based surveillance.

Collection of accurate population-based surveillance data for FAS is an important public health activity. In addition to providing an estimate of the public health burden of FAS, these data provide critical information to those planning clinical, behavioral, and educational interventions to support children with FAS and their families. Such services have been shown to reduce the risk for secondary conditions in this vulnerable population (7). Because many communities plan for service

www.nofas-uk.org

174
provision based on the prevalence estimates from records-based systems, the need for FAS specific treatments, interventions, and services might not be recognized.

Surveillance of FAS also provides the opportunity to measure the effectiveness of public health interventions aimed at reducing the number of children at risk for FAS because of in utero alcohol exposure. Alcohol consumption during pregnancy is common. During 2006–2010, 7.6% of pregnant women reported drinking alcohol, with 1.4% reporting binge drinking (8). Further, over 50% of pregnancies are unplanned (9), and alcohol exposure can harm the fetus even before the pregnancy is recognized (1). FAS surveillance could provide evidence of the effectiveness of approaches to reduce alcohol consumption during pregnancy. One primary prevention strategy is alcohol screening and brief intervention. A California study found that pregnant women who received alcohol screening and brief intervention at a social service agency were five times more likely to abstain from alcohol during the remainder of their pregnancy and delivered infants who were healthier on several newborn measures (10).

Recognition of children with FAS is critically important to ensure their access to appropriate services and interventions. However, identifying affected children through population-based surveillance continues to be a challenge. Prevalence estimates from the Fetal Alcohol Syndrome Surveillance Network II demonstrate that FAS is still underrecognized. Efforts that address the factors that contribute to this underrecognition might lead to practice changes, ultimately increasing recognition and documentation of the physical and behavioral characteristics of FAS. With increased recognition and documentation, records-based surveillance of FAS might yield estimates more similar to those based on in-person, expert assessment of school-aged children in a community.

Read Full Article

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6403a2.htm

Back to Table of Contents

---

E. Study Identifies Impacts of Women's Socio-Economic Status on Infant Health
Brenda McNally, Press Officer for the Faculty of Arts, Humanities and Social Sciences
16th January 2015

A new report from the Growing Up in Ireland (GUI) study, led by researchers at Trinity College Dublin, provides evidence of the profound influence of early life environment on children’s subsequent health and identifies implications for policy-makers.

The latest GUI study, which is the largest national study of children ever to take place in Ireland, has identified the longer term negative impacts of three specific maternal health behaviours on patterns of physical and mental health development in childhood. The study, entitled ‘Maternal Health Behaviours and Child Growth In Infancy’, was carried out by Professor Richard Layte, recently appointed Professor of Sociology in the Department of Sociology at Trinity College and Dr Cathal McCrory, Research Fellow, Centre For Medical Gerontology at Trinity College. The report was recently launched by the Minister for Children and Youth Affairs, Dr James Reilly.

Commenting at the launch, the minister said:

This report and its findings are a clear reminder that the prenatal period and the early years of a child’s life provide a unique window of opportunity to establish lifelong health and well-being patterns.
We must do what we can to protect children from harmful exposure to smoking in the prenatal and early childhood period and re-establish breastfeeding as the cultural norm in Ireland, thereby making it the natural choice for parents.

Pictured at the launch (l-r): Dr Cathal McCrory, Amanda Quail and daughter Ciara, Dr James Reilly and Professor Richard Layte

The GUI project is a government-funded study of children which aims to help improve understanding of all aspects of children and their development. The project involves a large nationally representative cohort study (20,000 children in total) and follows the development of two cohorts of Irish children, an Infant Cohort and a Child Cohort. The current findings were based on the Infant Cohort of over 11,000 children (undertaken between September 2008 and April 2009 when the children were 9 months old) and drew on data from the first wave of data collection from the study. The findings contribute to our knowledge of the impacts of prenatal and early-life environment on the subsequent health and well-being of older children.

Among the research findings, the report noted:

“Almost half of children were weaned onto solid foods before the guideline age of 6 months, although reasons for the early weaning were unclear.”

“Less breastfeeding and earlier weaning onto solid foods was associated with an unhealthy pattern of weight gain in infancy.”

The report also highlighted:

“The prevalence of early weaning in Ireland (before 6 months) suggests that parents in Ireland are not aware of the health consequences for their child. This reinforces the need for health professionals to communicate a clearer message on this issue to parents.”

Commenting on the policy implications of the findings, Professor Richard Layte said:

Poor child and maternal environment during pregnancy and infancy contributes to early ill health and may have life-long consequences. Research internationally shows that investment in maternity services and community health services saves money both in the short and long run.

The study investigated the extent and distribution of three specific health behaviours among mothers in the GUI study, namely cigarette smoking and alcohol consumption in pregnancy and extent of breast feeding. The researchers then examined the impact of these behaviours on children’s birth weight and subsequent growth and development from birth to 9 months of age. The findings show that maternal smoking and alcohol consumption in pregnancy and the level of breast feeding are strongly influenced by the social environment of the mother and also the mother’s mental health. According to the researchers, the findings have significant implications for child health policy, particularly in terms of the need for improvements in maternity and community health services.

Key findings from the Growing Up In Ireland Study:

Compared to women in the UK, women in Growing Up in Ireland were significantly less likely to report drinking during pregnancy, but if they did consume, they were likely to drink more heavily than their UK counterparts.

Women with higher levels of income and education were more likely to drink alcohol during pregnancy, but were more likely to drink in moderation.

The GUI study followed the progress of almost 20,000 children and their families – a Child Cohort (8,568 children) interviewed at nine years and 13 years of age and an Infant Cohort (11,134 children) participating at nine months, three years and five years of age.
F. FASD in Review examines a recent article by Ira Chasnoff, et al., in Pediatrics, titled “Misdiagnosis and Missed Diagnoses in Foster and Adopted Children with Prenatal Alcohol Exposure,” Volume 135, number 2, February 2015

March 2015

Although FASD prevalence is now estimated to be higher than previously thought (May et al., 2014), challenges exist in obtaining access to diagnostic services in the United States due to an overall lack of awareness and diagnostic capacity (Astley & Grant, 2014). In addition, even if diagnostic resources are available in a given community, many providers do not have sufficient awareness about FASD to conduct screening that could lead to a diagnosis (Grant et al., 2013). When an individual does find diagnostic services, challenges still exist in obtaining an accurate diagnosis, for reasons including diagnostic challenges related to the breadth of the spectrum, cases of unknown maternal history of alcohol use, lack of consistent facial dysmorphology and growth impairment across diagnoses within the spectrum, and the high rate of co-occurring mental health disorders that can complicate differential diagnosis (Chasnoff et al., 2015; Greenbaum et al., 2009). These challenges have wide-ranging consequences, including a lack of appropriate early interventions, leading to ineffective services and poor outcomes (Olson et al., 2007).

Read Full Article

FASD in Review

Back to Table of Contents
A. **Fetal alcohol test under development**

Article by Tracey Romero  
Publication - The Philadelphia Inquirer  
9th February, 2015

PHILADELPHIA — Alcohol is the leading known preventable cause of developmental and physical birth defects in the United States, according to Kidshealth.org, but despite that, many women still drink during pregnancy. About 1 in every 750 infants is born with fetal alcohol syndrome and another 40,000 with fetal alcohol effects.

To help identify damage to the fetus earlier so that better intervention is possible, a research team at Temple University School of Medicine is developing a test to identify maternal blood biomarkers that can assess fetal neurodevelopment in the first and second trimesters.

This project was a recent winner of Bill & Melinda Gates Foundation’s Grand Challenges Explorations grants. Temple was one 60 winners who will focus on solving persistent global health and development challenges.

Dr. Laura Goetzl, a professor of obstetrics, gynecology and reproductive sciences, and her research team will be working with the Shriners Hospitals Center for Neural Repair and Rehabilitation to develop a noninvasive maternal blood test that will help predict abnormal fetal neurodevelopment. Specifically they will be focusing on the effects of antidepressants, amphetamines and alcohol.

"We have been working on the effects of medication on the unborn fetus. Most of the available data is from the third trimester when everyone wants to know about early trimesters. Neural elements from the fetus can pass into the mother's bloodstream and may be able to be used to measure ongoing brain injury," Goetzl said.

Inspired by work with biomarkers in Alzheimer's research and noninvasive testing for Down syndrome, they will be using special technology to identify what biomarkers are released from the baby's brain and cross over the placenta into the mother's blood.

Goetzl and her team hope to be able to identify brain injury in the fetus early so that there can be intervention and reduction of injury, but a lot of work still needs to be done. The initial grant is for 18 months and that is just to see if such a maternal blood test is possible. It could take up to 10 years to really know how well the new test will correlate with developmental outcomes and whether it can be used going forward to prevent neural injury.

**Read Full Article**


Back to Table of Contents
B. Fetal alcohol test under development

Article by Neil Osterweil
Publication - Medscape Medical News
12th January, 2015

Children referred to a specialist because of behavioral problems may have undiagnosed fetal alcohol spectrum disorders (FASD), suggest results of a new study.

Among 547 foster or adopted children referred to a children's mental health center for behavioral issues, 156 met criteria for FASD, but 125 (80.1%) had never been diagnosed with prenatal exposure to alcohol, report Ira J. Chasnoff, MD; Anne M. Wells, PhD; and Lauren King, MA, from Children's Research Triangle in Chicago, Illinois.

Of 31 children who had been diagnosed with prenatal alcohol exposure before referral, 10 had a change in their diagnosis to a different disorder within the fetal alcohol spectrum, which represents a 6.4% misdiagnosis rate, the investigators said.

“Although FASD have long been recognized as a leading cause of intellectual disabilities, behavior problems, learning disabilities, and cooccurring mental health disorders, children and adolescents who have been affected by prenatal alcohol exposure often go undiagnosed or are misdiagnosed,” Dr Chasnoff and colleagues write in an article published online January 12 in Pediatrics.

The researchers collected data on a sample of 547 children referred to their center for multidisciplinary diagnostic evaluation. They used current diagnostic criteria to identify whether the children should have been diagnosed with FAS, partial FAS, alcohol-related neurodevelopmental disorder, or alcohol-related birth defects.

The investigators note that although children with FAS are usually correctly diagnosed on the basis of growth criteria, central nervous system impairment, and characteristic facial features, other, more common disorders related to prenatal alcohol exposure may be missed.

“Unfortunately, many children and adolescents with FASD go unrecognized and untreated; this is due to multiple factors, including unknown maternal history of alcohol use during pregnancy, lack of consistent facial dysmorphology and growth impairment across all diagnoses within the fetal alcohol spectrum, and the high rate of cooccurring mental health disorders,” the authors write.

They hypothesize that in addition to these factors, “the historically confusing language and diagnostic terminology applied to alcohol-affected children, and the perceived stigma against addressing alcohol use by pregnant women most likely contributed to the majority of affected children and adolescents in the current study having been misdiagnosed or missed completely.”

The authors point out that only half of American Academy of Pediatrics members surveyed reported being confident in their ability to make a FASD diagnosis and cited evidence that behavioral issues associated with prenatal alcohol exposure are often mistaken for attention-deficit hyperactivity disorder.

Other studies have shown that compared with children without FASD, children with prenatal alcohol exposure tend to have greater verbal and reasoning difficulties and exhibit higher levels of sociopathic behaviors such as stealing or lying, they explain.

Children and adolescents with FASD require “more intense forms of mental health therapy addressing attachment difficulties, behavioral difficulties, and sensory processing deficits,” the investigators write.

The study was supported in part by a grant from the US Department of Health and Human Services. The authors have disclosed no relevant financial relationships.
C. New warning over booze in pregnancy: Half a glass of wine 'could stop some babies breathing'

Sophie Borland, Health Correspondent for the Daily Mail
24 February 2015

- NHS guidelines say pregnant women can drink one or two units at most
- New study says even just half a glass of wine could damage a baby
- Scientists say babies stop breathing for up to two hours if mother drinks
- Experts compared drinking to Thalidomide which caused birth defects

Doctors said even just drinking half a glass of wine could stop babies breathing for up to two hours

Pregnant women are being urged not to drink at all after a study found that just half a glass of wine can stop their baby breathing and moving for up to two hours.

The research, which reveals the dangers of just one unit of alcohol, flies in the face of NHS guidelines.

These imply it is safe for pregnant women to continue drinking as long as it is not more than one or two units, once or twice a week.

Experts claim British women are being given insufficient advice, and compared the toxins in alcohol to those in Thalidomide – the infamous drug for morning sickness that caused severe birth defects in the 1950s and 60s.

Professor Peter Hepper, who carried out the study on the effects of low-level alcohol in pregnancy – the first of its kind in the UK – said: 'If women drink just one unit of alcohol, the baby's breathing and movement stop for up to two hours after that. That's not normal – the baby should be continually active.'

The professor, from Queen's University Belfast, looked at 18-week scans of pregnant women who drank on average two-and-a-half units a week – equivalent to a 200ml glass of wine.

He noticed the foetuses stopped moving and breathing, then they suddenly jumped and turned themselves over.

Speaking to ITV's Exposure programme, which will air next week, he said the jolts suggested the babies' brains were not developing properly. 'The only safe [alcohol] level is zero,' he added.

Dr Mary Mather, a consultant paediatrician, said British women were being 'deprived' of information about the dangers of drinking while pregnant.
In the US, Canada, Australia, New Zealand, Spain, Switzerland and the Netherlands, pregnant women are told not to drink at all.

Dr Mather said: ‘Alcohol is a poison... it’s toxic to developing tissue. It’s also what doctors call a teratogen. The best known teratogen is Thalidomide. It’s in the same category of drugs.’

Sir Al Aynsley-Green, a professor of child health at University College London and a former Children’s Commissioner, said: ‘Exposure to alcohol before birth is the single most important preventable cause of incurable brain damage.

‘There is insufficient reliable information that can help women make these important decisions.’

It is estimated that as many as one in 100 babies born in Britain have physical defects or behavioural problems caused by their mother’s drinking. This is known as Foetal Alcohol Spectrum Disorder and the condition lasts for life.

Dame Sally Davies, the chief medical officer for England, is currently reviewing the guidelines on safe drinking for all adults, including pregnant women. Her new advice is due this summer.

The Department of Health said: ‘Our advice is that pregnant women or women trying to conceive should avoid drinking alcohol. If they do choose to drink, to minimise the risk to the baby, they should not drink more than one to two units of alcohol once or twice a week and should not get drunk.’

Read Full Article
http://www.dailymail.co.uk/health/article-2965856/Protein-Eating-protein-strain-kidneys-little-bad-muscles-getting-right-amount.html

Back to Table of Contents

D. Das Fetale Alkoholsyndrom
Im Kindes- und Erwachsenenalter
[Fetal Alcohol Syndrome: Alcohol, Pregnancy, and Risks for the Developing Child]
Spohr, Hans-Ludwig

In collaboration with Wolter, Heike
With contrib. by Becker, Gela / Heinen, Florian / Landgraf, Mirjam / Nagel, Manuela / Siedentopf, Jan-Peter / Wagner, Jessica

The harmful consequences of alcoholism for the unborn child are still largely unknown. This book presents a detailed description of fetal alcohol syndrome as well as fetal alcohol spectrum disorders with respect to their clinical presentation, diagnosis, epidemiology, and pathogenesis. It also includes detailed considerations of underlying psychopathology, prevention, and therapy as well as the social consequences and impacts to patients.
E. Better-off women more likely to drink alcohol in pregnancy

Rachel Flaherty
Publication – the Irish Times
15th January 2015

Women with higher levels of income and education are more likely to drink alcohol weekly during their pregnancy, new figures have shown.

While more than one in 10 mothers (13 per cent) smoked all the way through their pregnancy, there was an increased risk of smoking linked to being poor and having lower levels of education.

The findings are from a new report, Maternal Health Behaviours and Child Growth in Infancy, published as part of the Growing Up in Ireland study.

The report draws on data from a cohort of 11,134 infants and their families.

Women with higher levels of education and income being more likely to drink alcohol in pregnancy was a “common finding internationally”, said Prof Richard Layte of the Economic and Social Research Institute (ESRI) and co-author of the report.

Acceptable risk

“As to why, we don’t have exact data on this. Clearly those women feel that it’s an acceptable risk. The guidelines in Ireland are women should not drink in pregnancy.

“There is no strong evidence at the moment that low consumption of alcohol has a long-term impact on the child. That might be wrong, just the studies haven’t shown yet. We are reliant on observational studies,” he said.

“They tend to be more regular drinkers but quite less likely to binge-drink. A unit is about a glass of wine, not very strong wine, or half a pint of beer, of not very strong beer,” he said.

About 10 per cent of the women in the study drank alcohol and about 7 per cent of those drank under two units a week, he said, adding that 3 per cent of women in the study reported they drank more than two units of alcohol a week.

Prof Layte said there was a link between women who smoked and drank alcohol in pregnancy.

“Women who smoke are more likely to drink during pregnancy.

“It’s quite rare for someone who will smoke and not consume alcohol in some level. That’s not to say they drink to excess.”

Social circumstances
The statistics showed women who experienced “a great deal of stress” were 37 per cent more likely to smoke. Prof Layte said the social circumstances were very important influencers on a pregnant woman’s health behaviours.

The study showed if a woman’s partner continued to smoke during the pregnancy, the mother was 70 per cent less likely to quit.

“Even if she stops smoking, the child’s birth weight will still be lower as a result of the passive smoking.” Prof Layte said the figure of 13 per cent of women in Ireland continuing to smoke through their pregnancy was about average with Europe.

The study also found the proportion of women in Ireland who smoked at all in pregnancy dropped from 28 per cent in 1999 to 17 per cent in 2007.

**Read Full Article**


**Back to Table of Contents**

---

**F. Drinking in pregnancy 'significant' cause of childhood brain damage**

Article by Eleanor Bradford, BBC Scotland Health Correspondent

23rd June 2015

One of the UK’s leading experts in child health is calling for stronger warnings on alcohol to alert women to the dangers of drinking while pregnant.

Sir Al Aynsley-Green said exposure to alcohol before birth was one of the "most significant" causes of childhood brain damage.

His call for tougher labelling was backed by delegates at the British Medical Association annual conference.

Sir Al has called for all UK governments to raise public awareness.

Foetal Alcohol Syndrome is a condition affecting children whose mothers drank while pregnant.

Sir Al is the emeritus professor of child health at University College London, honorary fellow of Oxford University and the first children's commissioner for England.

He said: "Exposure to alcohol before birth is one of the most significant causes of childhood brain damage, learning disability, poor behaviour and even criminality, affecting up to one in every 100 infants."

"It is entirely preventable by not drinking alcohol during pregnancy, but despite this, advice to expectant mothers in the UK and especially England is inconsistent, contradictory and confusing, and services to support diagnosis and management of affected children are inadequate.

“There has, however, been political denial of the scale and importance of the problem."
Scottish Public Health Minister Maureen Watt said the Scottish government was developing a "consistent diagnostic tool" to allow it to accurately record the number of foetal alcohol syndrome cases.

She said the government were monitoring the number of cases and would be able to publish the results in Autumn 2015.

Ms Watt said: "We do not currently have foetal alcohol syndrome teams in any hospital in Scotland."

However, she said they were studying the methods of identifying and treating FAS used in other countries.

Susannah Mackay said it could affect the relationship between the child and its mother

Susannah Mackay, from Dundee, has an adopted son and foster daughter who have both been diagnosed with disorders related to exposure to alcohol while in the womb. Her son was placed with her when he was seven and her daughter when she was six.

"My daughter has classic Foetal Alcohol Syndrome - not that it was diagnosed when I took her on," she said.

"My son is more impulsive. He has Foetal Alcohol Effects. It took two and a half years from their placement to get a definite diagnosis. They were eventually diagnosed by geneticists who ruled everything else out."

It is not known exactly how many children suffer from Foetal Alcohol Spectrum Disorders (FASD) but the condition is widely under-diagnosed.

Some children will display tell-tale facial features, with a 'pixie' like appearance, but many more will have brain damage which is hidden until they grow older and go to school.

Prof Bill Phillips has specialised in foetal alcohol spectrum disorders for many years

Prof Bill Phillips is an academic and research scientist who has specialised in foetal alcohol spectrum disorders for many years.

"When a baby is born and it looks fine, it doesn't follow that the brain isn't affected," said the emeritus professor at the University of Stirling.

"The face is only affected if there's excessive drinking early in development - during the first three months. The brain goes on developing and drinking can affect the brain at any time."

"It makes the brain less able to regulate its activity, more impulsive, less able to ignore distractions and less able to plan behaviour according to long term goals."

"It affects all aspects of their life," said Mrs Mackay.

"They have very poor impulse control. They never think about consequences. They can't manage time or money. They lack emotional maturity. I might tell them something one day and have to tell them again the next day, and the next day."

Rena Phillips said foetal alcohol syndrome was a ticking time-bomb

Prof Phillips' wife, Rena, is a social worker, a support group organiser and sits on Children's Panels - legal tribunals which make decisions on the care of vulnerable children in Scotland.

"It's a ticking time-bomb which has kind of exploded," she said.

"Talking to my colleagues, we reckon that the majority of children who come before children's panels have substance misuse in the background. It's in 80% to 90% of cases."

"Unfortunately we've had examples where children have been placed for adoption and the adoptive parents didn't know about the abuse of alcohol during pregnancy.
"Health professionals in health and education don't have enough knowledge about this and they should be told because then they can deal with the consequences."

Drinks manufacturers are encouraged to include "sensible drinking" information for pregnant women on its labels, including warnings to women to "avoid" alcohol if pregnant or trying to conceive.

However such labels are not mandatory.

The Portman Group, which represents the drinks industry, said: "While it is a matter for government to determine safe drinking guidelines, alcohol companies strongly advocate that women should avoid alcohol if pregnant or trying to conceive, which is why the industry has voluntarily labelled over 90% of products on shelves with this advice.

"Calling for legislation in this area is completely unnecessary."

The question of how much alcohol damages the foetus is hotly debated.

Excessive consumption

The Royal College of Obstetricians and Gynaecologists has said "current scientific opinion points to there being no hard evidence that very small amounts of alcohol consumption during pregnancy are harmful".

However, others argue that there is growing scientific evidence that there is no safe limit.

"In contrast to places like Canada, where there is widespread awareness of the risks, and provinces provide comprehensive assessment and prevention support, in England there is little debate or political interest in the effects of drinking during pregnancy, despite a worrying culture of excessive alcohol consumption," said Sir Al.

Prof Phillips agreed.

He said: "If you want a large effect you drink a lot, if you want a little effect you drink a little. If you want no effect you don't drink at all."

Mrs Mackay said that as her children have grown into young adults they have realised that their difficulties could have been avoided.

She said: "It makes it hard to have a relationship with their birth mums, but they both do.

"It's hard to think 'I am the way I am because of what you did'.

"That causes them emotional problems. I don't think they blame their mums because it's a circumstance of their birth, but if they had a choice would they be the way they are? Probably not."

Read Full Article

http://www.bbc.co.uk/news/uk-scotland-33230201

Back to Table of Contents
G. ITV Documentary
Exposure: When Pregnant Women Drink

“Exposure to alcohol before birth is the single most important preventable cause of incurable brain damage. And it’s an issue which affects all of us in society.” - Professor Sir Al Aynsley-Green, former Children’s Commissioner for England

Ranvir Singh investigates the impact of drinking alcohol in pregnancy as one in 100 babies are born in Britain each year brain-damaged with Foetal Alcohol Spectrum Disorder (FASD).

These babies will go through life with a range of developmental, social and learning difficulties. A few will have tell-tale facial features which will make it easier to get a diagnosis and access support, but the majority will battle with an invisible disability.

Exposure meets four people affected by FASD to understand their challenges and the impact on their families.

- James is five and his adoptive parents are on the path to a diagnosis so that he can get the help he needs. He undergoes ground-breaking 3D facial analysis with Professor Peter Hammond which can detect the facial traits of Foetal Alcohol Syndrome that are invisible to the naked eye.

- Jade is lively, articulate and talented – she is also trusting, impulsive and volatile. Being a teenager is tough, for Jade being a teenager with FASD brings a whole raft of other problems.

- Sam drank a lot through her pregnancy but tells Exposure that she was never warned of the dangers to her baby. Stanley is now 11. His life is changed forever as a result of what happened when he was in the womb. Understandably, he can be an angry young man.

- Lee was 26 when he received his diagnosis and had already served a prison sentence for a violent crime.

The Government’s current guidelines advise that those who are pregnant or trying to get pregnant should avoid alcohol altogether – but then adds, ‘If women do choose to drink, to minimise the risk to the baby, we recommend they should not drink more than one to two units once or twice a week and they should not get drunk.’

The Royal College of Obstetricians and Gynaecologists had taken a similar view, although they referred to one or two units a week as a safe amount. Spokesman Dr Pat O’Brien says: “If nobody drank any alcohol in pregnancy there would be no Foetal Alcohol Syndrome and no Foetal Alcohol Spectrum Disorder. But on the other hand if you look at all of the evidence there appears to be a safe level of alcohol intake in pregnancy.”

However earlier this month they updated their advice, recommending that pregnant women do not drink alcohol during the first three months of pregnancy. The advice does say that drinking small amounts of alcohol after this time does not appear to be harmful for the unborn baby, but that pregnant women should not drink more than one or two units, and then not more than once or twice a week.

The Department of Health declined an interview and gave a statement outlining their current advice and stating that the Chief Medical Officer is currently reviewing the guidance on drinking alcohol.

Ranvir brings together a group of pregnant women from around the country to find out what they have been told about the risks of alcohol in pregnancy. All of these women are following the current NHS guidelines and some have chosen not to drink at all while pregnant. Some were given no information on alcohol, while others found the guidelines confusing and contradictory.

Prof Peter Hepper of Queen’s University, Belfast has carried out the only UK research on the impact of low levels of alcohol on the foetus. When Exposure shows this to the pregnant women, they are shocked to discover that even when drinking just one unit of alcohol - well within the government guidelines - the
Exposure compares the position in the UK to overseas where for more than 30 years the advice to women in the US has been that pregnant women should not drink at all during pregnancy.

Critics of the UK guidelines view this as a clear and unambiguous message, which is also promoted by many other countries among them Australia, Canada, New Zealand, South Africa, France, Germany, Spain and the Netherlands. Exposure also hears that research was carried out in the US in 2013 that revealed alcohol is more damaging to a foetus in the womb than heroin, cocaine, cannabis or smoking.

Dr Raja Mukherjee, lead clinician at the only NHS clinic specialising in FASD, tells Exposure that alcohol affects brain development in the foetus at every stage of a pregnancy, resulting in brain cells being killed off, in the wrong place or missing altogether.

“What's it's doing is it's stopping normal development, it's interfering with the process, so you've got brain cells being killed off, you get brain cells in the wrong place, you've got parts of the brain that just are absent.”

Consultant Paediatrician Dr Mary Mather believes there is no safe limit of alcohol to drink and pregnant women need to know this. She says the only way to guarantee a child will not have FASD is not to drink.

“Alcohol is a poison, it's a toxin, it's toxic to developing tissue and it's also what doctors call a Teratogen. And the best known Teratogen is obviously Thalidomide.”

“Well I think they [pregnant women] probably should be panicked. This is an incurable lifelong disability. I think it's time the professionals started to give pregnant women clear advice about the real risks in pregnancy.”

This point of view is supported by Prof Sir Al Aynsley-Green as he explains new research shows that some mothers clear alcohol from their bloodstream faster than others and it's these unknown and individual differences that may explain why some babies are affected more than others.

He says: “I've got great empathy and sympathy for women today in the UK because the advice they are getting is not consistent, it is confusing and they're getting different opinions so it's not surprising that many of them, too many of them are confused, worried and anxious and it's time we clarified the situation. In my view there is insufficient, reliable, accurate information that can help women to make these important decisions.”

As the Chief Medical Officer is currently reviewing all guidelines for drinking alcohol – many argue now it is time to bring British advice on alcohol and pregnancy into line with those countries who advocate no alcohol at all.

Watch ITV documentary:
http://www.itv.com/presscentre/ep1week10/exposure-when-pregnant-women-drink

Back to Table of Contents
Antenatal alcohol exposure: An East Anglian study of midwives’ knowledge and practice

Abstract

Objective: To study midwives’ knowledge, practice and opinions regarding advice about fetal alcohol syndrome (FAS), fetal alcohol spectrum disorders (FASDs) and alcohol intake in pregnancy.

Design: A postal questionnaire was sent to 1862 midwives employed in 13 NHS Trusts in East Anglia, incorporating city and rural areas.

Results: The authors received responses from 33.5% of the midwives contacted (n=624), of which 98% stated that alcohol abstinence in pregnancy would be their preferred advice, and 38% had seen an infant with FAS. Less than 2% indicated that they were ‘very prepared’ to deal with the subject. Only 10% identified all four classic features of FAS.

Conclusions: More than a third of midwives had seen an infant with FAS. The advice given to pregnant mothers by participants varied. The midwives stated that they would like more information and support.

Implications for practice: Expansion of midwives’ knowledge should improve the quality of antenatal advice, leading to better prevention, intervention and recognition of FASD in children.

Keywords: Fetal alcohol spectrum disorder, Fetal alcohol syndrome, Pregnancy, Alcohol, Midwifery practice

In 1968, the French doctor Lemoine and his colleagues first described a pattern of physical and neurodevelopmental abnormalities observed among children of mothers with alcohol problems (Lemoise et al., 1968). Unfortunately, this series of French case studies went unnoticed until Jones et al. (1973) publicised their independent observations in the USA 5 years later. Jones et al. (1973) introduced the term ‘fetal alcohol syndrome’ (FAS) to describe common features of the disorder.

FAS is a complex, multifactorial disorder in which exposure to alcohol consumption interacts with other environmental and genetic factors. Two developments in research have suggested further complications (National Perinatal Epidemiology Unit, 2006):

- Recognition that it is possible to have partial forms of the syndrome, i.e. fetal alcohol spectrum disorders (FASDs)
- Evidence that a more moderate alcohol consumption may also be harmful to the developing fetus.

The worldwide incidence of FAS is 0.07 cases per 1000 births, making it the most common cause of non-genetic learning disabilities around the world. Western countries report a FASD diagnosis in as many as 9 cases per 1000 births; therefore, the condition is of global concern (British Medical Association (BMA), 2007).

The prevalence of FASD is unknown in the UK as there is no standardised approach to making and recording the diagnosis—this highlights the need for a UK-wide epidemiological study. Other countries, including Canada, the USA and Australia have collected FAS data (Williams et al., 1999; May and Gossage, 2001; Chudley et al., 2005; Elliott et al., 2007).

The diagnosis of FASD relies on history-taking and clinical examination because there is no diagnostic test available. The two main diagnostic criteria systems in use originate from the USA and are intended for use in the clinical setting: the Institute of Medicine (IoM) Criteria, by Stratton et al. (1996), and the Centers for Disease Control and Prevention (CDC) Criteria, by Bertrand et al. (2014). For diagnosis, prenatal alcohol exposure should be ascertained or assumed, and during a clinical assessment, the health professional should concentrate on identifying a triad of the following (not all need to be present):

- Specific facial features
- Growth restriction
- Neurodevelopmental disorder.

The provision of advice for women about alcohol intake presents a dilemma for midwives and obstetricians, who do not wish to spread alarm but recognize the need for information. Accurate history-taking by midwives is crucial to identifying women at risk, hence the authors’ interest in exploring midwives’ knowledge and practice relating to their advice about alcohol consumption during pregnancy.

Existing UK guidelines

The evidence and the antenatal guidelines on which midwives base their advice were reviewed. The BMA (2007), following an extensive review
in 2007 that aimed to raise awareness of FASDs, stated: ‘Women who are pregnant, or who are considering a pregnancy, should be advised not to consume any alcohol.’

The Department of Health recommends that pregnant women should avoid alcohol altogether (NHS Choices, 2014). However, the National Institute for Health and Care Excellence’s (NICE) antenatal care guideline is different. It dates from 2003, was updated in March 2008, and was reviewed again in March 2011. It was then placed on the ‘static list’, meaning the advice stays as it is but will be reviewed every 5 years (NICE, 2003; 2008). NICE recommends that:

- Pregnant women and women planning to become pregnant should be advised to avoid drinking alcohol in the first 3 months of pregnancy because there may be an increased risk of miscarriage.
- Women should be advised that if they choose to drink alcohol while they are pregnant, they should drink no more than 1-2 UK units once or twice a week.
- Women should be advised not to get drunk or binge drink (drinking more than 7.5 UK units of alcohol on a single occasion) while they are pregnant as this can harm their unborn baby.

The Royal College of Obstetricians and Gynaecologists (RCOG) recently produced (February 2015) a patient information leaflet giving advice about the effects of drinking alcohol during pregnancy. This was based on the above NICE guideline. RCOG stated that the only way to be certain that the baby is not harmed by alcohol is to abstain from drinking during pregnancy or while breastfeeding. The Royal College of Midwives (RCM, 2015) commented on the leaflet and said: ‘The evidence suggests that the cumulative effects of alcohol consumption during pregnancy cause harm to the developing fetus and can have adverse impacts on the newborn. The RCM continues to advise women to abstain from drinking alcohol when pregnant or if trying to conceive.’

**Methods**

This quantitative, non-experimental study was designed to discover what advice practising midwives give about alcohol intake in pregnancy. The questionnaire used for the study was closely based on one distributed in Western Australia to 1,443 health professionals (75% participated) in 2002–2003; written permission from the authors of this study was obtained.

Section one explored demographic data, current knowledge and practice regarding FAS, sources of information, preparedness and available resources.

**Table 1. Year of midwives’ graduation**

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>1966-1980</td>
<td>80</td>
</tr>
<tr>
<td>1981-1995</td>
<td>238</td>
</tr>
<tr>
<td>1996-2011</td>
<td>290</td>
</tr>
<tr>
<td><em>16 midwives did not reply</em></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Midwives’ areas of work**

<table>
<thead>
<tr>
<th>Midwife type</th>
<th>Number of respondents</th>
<th>Percentage of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital midwife</td>
<td>268</td>
<td>43%</td>
</tr>
<tr>
<td>Community midwife</td>
<td>257</td>
<td>41%</td>
</tr>
<tr>
<td>Midwife (other)</td>
<td>99</td>
<td>16%</td>
</tr>
</tbody>
</table>

**Table 3. Midwives seeing infants**

<table>
<thead>
<tr>
<th>Infants seen per week</th>
<th>Percentage of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not see any infants</td>
<td>9%</td>
</tr>
<tr>
<td>Saw between 1–25 infants</td>
<td>81%</td>
</tr>
<tr>
<td>Saw between 26–35 infants</td>
<td>6%</td>
</tr>
<tr>
<td>Saw between 36–50 infants</td>
<td>4%</td>
</tr>
</tbody>
</table>

**Table 4. Midwives seeing pregnant women**

<table>
<thead>
<tr>
<th>Pregnant women seen per week</th>
<th>Percentage of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not see any pregnant women</td>
<td>0.16%</td>
</tr>
<tr>
<td>Saw between 1–30 pregnant women</td>
<td>80%</td>
</tr>
<tr>
<td>Saw between 31–60 pregnant women</td>
<td>18%</td>
</tr>
<tr>
<td>Saw between 61–100 pregnant women</td>
<td>1.84%</td>
</tr>
</tbody>
</table>

Section two explored midwives’ opinions, perceived educational needs and attitudinal perspectives, using a Likert scale.

In 2007, there were 35,305 midwives in the UK (Nursing and Midwifery Council (NMC), 2007). The Centre for Applied Medical Statistics (CAMS), University of Cambridge, stated that 600 midwives were needed to participate to ensure robust data. This study recruited midwives from NHS Trusts in East Anglia.

Ethical approval for the research was gained from the Cambridgeshire Research Ethics Committee in November 2010 (reference: 10/H0905/54). In addition, the study was discussed with the Research and Development Department and the audit coordinator. Final midwifery management and Research and Development approvals were gained from each NHS Trust via Site-Specific Information (SSI) forms by March 2011.
Table 5. Respondents’ knowledge of features of fetal alcohol syndrome

<table>
<thead>
<tr>
<th>Knowledge of the four essential features</th>
<th>Percentage of respondents</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>CNS abnormality/dysfunction</td>
<td>46%</td>
<td>54%</td>
</tr>
<tr>
<td>Abnormal facial appearance</td>
<td>64%</td>
<td>36%</td>
</tr>
<tr>
<td>Growth restriction</td>
<td>55%</td>
<td>45%</td>
</tr>
<tr>
<td>Confirmed prenatal alcohol intake</td>
<td>54%</td>
<td>46%</td>
</tr>
<tr>
<td>Midwives who ticked all four correct features and no others</td>
<td>10%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Note: Choices were not mutually exclusive; CNS—central nervous system

Table 6. Experience with fetal alcohol syndrome

<table>
<thead>
<tr>
<th>Experience of FAS</th>
<th>Percentage of respondents</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Had diagnosed FAS</td>
<td>4%</td>
<td>96%</td>
</tr>
<tr>
<td>Had seen already diagnosed child with FAS</td>
<td>34%</td>
<td>66%</td>
</tr>
<tr>
<td>Certain child had FAS but did not record</td>
<td>&lt;1%</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Referred children to confirm a diagnosis of FAS</td>
<td>3%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Note: Choices were not mutually exclusive; FAS—Fetal alcohol syndrome

As the questionnaire was anonymous, it was not possible to document signed consent. Consent was assumed if the questionnaire was returned. The first page of the questionnaire explained the research purpose, gave clear instructions and invited the midwives to participate. There is great variation in the demographics of the East Anglian population, so it was important that the geographical distribution of the responses was identified, otherwise the findings could be skewed. It was made clear to respondents that it would be possible to identify the Trust from which the response came.

Midwives were not coerced to participate, although a polite reminder was emailed to the entire sample group via their Trusts; 13 NHS Trusts in East Anglia participated and 1862 questionnaires were distributed.

The coded, quantitative study data were stored on a password-protected computerised database, and the response to each question was given an individual value with a label for identification, including missing values.

Of the questionnaires distributed, 624 were completed satisfactorily, resulting in a response rate of 33.5% by August 2011.

Statistical analysis used descriptive statistics and PASW (formerly Statistical Package for the Social Sciences (SPSS)), version 17, with advice from CAMS.

To make analysis more meaningful, the Likert scale-based attitudinal questions were mostly grouped, i.e. ‘strongly agree’ with ‘tend to agree’.

The qualitative data obtained from the free text boxes were coded into themes, and the frequency of themes was considered (see Results). Test-retest should be possible for a replication of the study.

Results

Respondents’ characteristics

The entire respondent group was female; 268 respondents were hospital-based midwives, 257 were community midwives, and 99 worked in a variety of roles. They graduated between 1966 and 2011; the majority graduated after 1980 (86.8%) and less than 4% graduated before 1973, when FAS was first described in English (Jones et al, 1977). The respondents saw a wide range of pregnant women and/or infants in a typical week, as shown in Tables 2–4.

Participants’ knowledge

Midwives were asked how they gained their knowledge and awareness of FAS, and most (82%) stated that this was from professional training/studies. Table 5 outlines participants’ knowledge of the four essential features of FAS, according to Astley and Clarren (2000):

- Central nervous system (CNS) abnormality/dysfunction
- Abnormal facial appearance
- Growth restriction
- Confirmed alcohol exposure in pregnancy.

Additionally, two non-essential features were listed as ‘red herrings’. Just 10% of the respondents correctly identified all four diagnostic features.

Around 4% of midwives had previously diagnosed FAS, and 34% had seen an infant with an established FAS diagnosis (Table 6), while 3% of respondents suspected and referred children to confirm a diagnosis. Less than 6% considered FAS a likely diagnosis but did not record it in medical notes.

Alcohol intake in pregnancy

The midwives were questioned on what they ask women about their alcohol habits, and, if women sought prenatal alcohol advice from them, and if they told women about the consequences of alcohol intake in pregnancy (Table 7). The aim was
to establish if midwives provided this information and if their practice reflected advice from current BMA (2007) and NICE (2008) guidelines. The questionnaire allowed respondents to tick more than one of the alternatives offered, so the answers were not mutually exclusive. Of the participants, 93% preferred to give the advice that pregnant women should consider not drinking alcohol at all; 27% suggested ‘do not become intoxicated’; 4% recommended drinking less than two units once or twice a week; and 3% advised ‘do not binge-drink’ (i.e. drinking five or more drinks). Many midwives did not provide advice in accordance with the latest NICE guidelines (2008). Despite most trusts having a mandatory question in antenatal notes, only 60% of the respondents said they routinely ask pregnant women about their alcohol use, and just 17% stated that they asked if there were certain known risk factors, i.e. alcohol and/or drugs. Disappointingly, only 29% routinely provided information about antenatal alcohol use, and 22% did not provide any information; however, >97% said that education and information on this subject should be readily available. The participants tackled difficult tasks: 74% emphasised the dangers of drinking to women, and 58% stated that they had needed to advise someone who was concerned about endangering their unborn child by drinking alcohol.

Some questions encouraged participants to use free text and about 5% volunteered information:

- ‘Have any resources assisted you in dealing with FAS?’ ‘Colleagues’ (n=11), ‘Training’ (n=9), ‘Literature’ (n=8), ‘Internet’ (n=7)
- ‘What affects your alcohol assessment skills in pregnant women?’ ‘I don’t have concerns discussing alcohol’ (n=10), ‘Guidelines keep changing’ (n=2), ‘Need an evidence-based leaflet for service users’ (n=2), ‘Women underestimate how much they actually drink’ (n=1).

The latter part of the questionnaire examined midwives’ confidence, opinions and perceived educational needs. A Likert scale was used, although these attitudinal questions essentially did not have ‘correct answers’, they provided an interesting insight into participants’ views (Table 8). Of the respondents, 85% believed that making an early diagnosis might help a child with FAS, and 84% agreed that FAS was preventable, although 52% believed that making a diagnosis might stigmatise the child and/or the family. When asked if professionals were sufficiently aware of FAS, 21% agreed, 62% disagreed and 17% were unsure.

When asked about their discussions with pregnant women, 75% of respondents felt it was easy to ask pregnant women about alcohol use, but

<table>
<thead>
<tr>
<th>Table 7. Alcohol intake in pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Choices</strong></td>
</tr>
<tr>
<td><strong>Midwives preferred choices about giving antenatal alcohol use advice</strong></td>
</tr>
<tr>
<td>Consider not drinking at all</td>
</tr>
<tr>
<td>Drink no more than one to two UK units once or twice a week</td>
</tr>
<tr>
<td>Don’t become intoxicated</td>
</tr>
<tr>
<td>Have less than four UK units over a week</td>
</tr>
<tr>
<td>Avoid drinking &gt; 5 standard drinks or 7.5 UK units on a single occasion</td>
</tr>
<tr>
<td><strong>Midwives asking women about antenatal alcohol use</strong></td>
</tr>
<tr>
<td>Routinely ask</td>
</tr>
<tr>
<td>Ask if a known risk factor exists [alcohol or drugs]</td>
</tr>
<tr>
<td>Do not ask</td>
</tr>
<tr>
<td><strong>Midwives providing antenatal alcohol use information</strong></td>
</tr>
<tr>
<td>Routinely provide information</td>
</tr>
<tr>
<td>Sometimes provide information</td>
</tr>
<tr>
<td>Provide information if a risk factor exists [alcohol and drugs]</td>
</tr>
<tr>
<td>Do not provide information</td>
</tr>
</tbody>
</table>

Note: Categories were not mutually exclusive.
Table 8. Opinions on fetal alcohol syndrome

<table>
<thead>
<tr>
<th>Statement</th>
<th>Percentage of respondents</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Agree*</td>
<td>Disagree*</td>
</tr>
<tr>
<td>Early FAS diagnosis of the child may improve treatment</td>
<td>85%</td>
<td>2%</td>
</tr>
<tr>
<td>It is possible to prevent FAS</td>
<td>84%</td>
<td>5%</td>
</tr>
<tr>
<td>FAS diagnosis may lead to stigmatisation</td>
<td>52%</td>
<td>19%</td>
</tr>
<tr>
<td>Health professionals are sufficiently aware of FAS</td>
<td>21%</td>
<td>62%</td>
</tr>
<tr>
<td>A safe level of alcohol in pregnancy has not been established</td>
<td>76%</td>
<td>15%</td>
</tr>
<tr>
<td>It is easy to ask pregnant women how much and how often they drink alcohol</td>
<td>75%</td>
<td>22%</td>
</tr>
<tr>
<td>Discussing alcohol use in pregnancy will frighten or anger pregnant women</td>
<td>6%</td>
<td>85%</td>
</tr>
</tbody>
</table>

FAS—Fetal alcohol syndrome. *Categories ‘Strongly agree’ and ‘Tend to agree’, and ‘Strongly disagree’ and ‘Tend to disagree’ were combined.

6% felt that discussing alcohol use could frighten or anger pregnant women. Many respondents (76%) agreed that there is no established safe level of alcohol intake in pregnancy. Participants were asked about their preparedness to deal with FAS and resources that would be helpful in dealing with parents and babies in this area of health care (Table 9).

Only 11 (5%) midwives felt ‘very prepared’ to deal with this area of health care, while 63 (30%) felt ‘fairly prepared’, 153 (25%) felt somewhat prepared, 395 (63%) were ‘not very prepared’ and 2 (0.3%) were not sure (Figure 1).

Discussion

This survey explored midwifery practice in East Anglia, in an area of health with little pre-existing research to guide practitioners and pregnant women. Similar studies from Australia (Payne et al, 2005) and Denmark (Kesmodel and Kesmodel, 2011) are frequently referred to and will hereafter be referred to as ‘the Australian’ or ‘the Danish’ study.

The findings indicate that accurate knowledge on diagnostic features of FAS is limited. The same uncertainty was apparent in the Australian survey, as just 12% of participants defined FAS correctly, compared with 10% in the East Anglia study. Children with FAS have a range of developmental, cognitive and communication problems that can benefit from early intervention strategies, so it is important that health professionals recognise the features (Stratton et al, 1996). Chudley (2008: 721) made the point that FAS is difficult to identify, while the wider spectrum of FASD is even more complex because there are no fully reliable diagnostic tests; ‘some rare diseases are rare simply because they are rarely diagnosed’.

It is therefore significant that 34% of the midwives who participated in the survey had seen an infant with the diagnosis of FAS; additionally, 4% had diagnosed an infant with FAS themselves compared with 5% in the Australian study. This is even more remarkable given that midwives usually only provide postnatal care for infants for the first 28 days of life and that the reported FAS diagnosis median age was 3.3 years in another Australian study (Elliott et al, 2007).

Ambiguous recommendations made it difficult for the midwives in East Anglia to give sound advice. This is entirely consistent with the Danish study (2000), which found that none of its sample knew the official recommendations, and the Australian study (2009), in which only 13% of health professionals adhered to official recommendations.

In Australia, the 2001 guideline was changed in 2009 (Australian Government, 2009) to: ‘Not drinking in pregnancy is the safest option’. Payne et al (2014) reported that in 2013, 99.4% (n=166) of midwives gave such advice, concluding that: ‘The 2009 guideline is easy to convey and reduces confusion when counselling pregnant women.’ Likewise, Denmark changed its guideline recommendations to abstinence in 2007, resulting in improved understanding (Kesmodel and Kesmodel, 2011). Midwives based in the UK may find it difficult to discuss these sensitive issues without clear consensus between advisory bodies, such as the BMA and NICE. The BMA guideline (2007) advises that women completely avoid alcohol in pregnancy, whereas the NICE guidelines (2008) present a number of options. Previous research established that women do not hold it against midwives if no accurate answer exists, but women appreciate frank discussions (Kirkham, 1997; Raymond et al, 2009). In the present study,
60% of East Anglian participants routinely asked all pregnant women about their alcohol use, compared with 59% in the Danish study, and 45% in the Australian study—in Australia, this increased to 93% by 2013 (Payne et al., 2014).

Of the midwives questioned in East Anglia, 93% stated that 'consider not drinking at all' best represented their preferred advice to give pregnant women, and this is in line with recommendations from the BMA (2007).

In East Anglia, just 20% of midwives (and 30% in the Australian survey) provided information about antenatal alcohol use if there was a known risk factor, suggesting a reluctance to discuss alcohol. This reluctance was also apparent in the Danish study, and all three studies reported that participants felt unprepared to deal with this topic. Midwives may not be afraid to facilitate support but seemed unsure about the most effective way to do so. Less than 2% (n=1) of participants felt 'very prepared' to deal with the area of FAS (and also just 2% of midwives in the 2005 Australian survey). In Australia, Payne et al. (2014) found that by 2013, most midwives felt confident in advising on alcohol in pregnancy; however, 93% stated that they would still like more education about FASD. The importance of education and involvement with multidisciplinary teams, the support of local government and a willingness to raise public awareness are crucial if this growing area of concern is to be addressed (Astley and Clareen, 2000). Brief interventions and discussion show promise for alcohol risk reduction in antenatal care (Stade et al., 2009; Wilson et al., 2012).

Despite debate about binge-drinking in the British media, just 23% (n=82) of East Anglian respondents stated that they would advise pregnant women to 'avoid drinking five or more drinks per session', and 27% indicated that they would advise women not to become intoxicated. This is in stark contrast to the Danish survey where 90% advised against binge-drinking.

Just 26% of respondents routinely provide information on alcohol, despite more than 37% of midwives agreeing that information should be readily available. In response, one author of the study produced a 'midwives' pocket guide', accompanied by a letter to participating midwives, which discussed the principal findings of this study. The pocket guide was designed so that midwives can discuss the front page with pregnant women, while the back page acts as an aid for health professionals.

### Advantages and limitations of the study

The strengths of this study include an acceptable response rate of over 30% from a number

| Table 9. Respondents’ opinions on helpful resources |
|---------------------------------|---------------------------------|-----|
| Resource                        | Percentage of midwives agreeing with helpfulness of resource | n |
| Written information for pregnant women | 76% | 476 |
| Pregnancy/alcohol history checklists | 48% | 297 |
| FAS materials for health professionals | 61% | 507 |
| FAS diagnostic checklist | 66% | 410 |
| Counselling and alcohol assessment training | 54% | 337 |
| Registry of specialists | 44% | 274 |
| Referral resources | 62% | 388 |

FAS: Fetal alcohol syndrome

of East Anglia NHS Trusts and the use of a questionnaire based on one that had already been successfully used in Australia. Interesting data were collected on a subject of great importance to public health, and a comparison was made with similar studies that had taken place in other countries, in this under-researched area in the UK (Larcher and Brierley, 2014).

However, caution must be taken when comparing this study’s results with others because of differences in the samples’ composition and culture. The results from East Anglia may also not be representative of midwifery practices throughout the UK.

### Recommendations for clinical practice and further research

An epidemiological study of FASDs across the UK would help to raise awareness of the issues discussed in this paper and would provide essential data for service planning. There are difficulties in setting up a robust population-based surveillance system for FASDs, such as agreeing a reliable surveillance case definition and obtaining an accurate history of alcohol intake in pregnancy. However, surveillance for FAS is currently carried out in Scotland, so it is possible that it could be carried out more widely across the UK.

Motivation for behavioural change is generally high during pregnancy (Larsson, 1983; Health and Social Care Information Centre, 2008); the greatest challenge may be knowing how best to motivate and inform pregnant women.

Complex issues require complex solutions; different strategies should be used to reach different populations, to encourage pregnant women to make use of personalised information, advice and support.
RESEARCH

Key points

- Worldwide studies have shown that the consumption of alcohol in pregnancy causes fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorders (FASDs), which may be under-diagnosed causes of disability in children.
- Most of the participating midwives felt uncertain in this area of health promotion.
- Midwives stated that they would benefit from readily-available information and resources if the best outcome for pregnant women is to be achieved.
- Outcomes could be improved by routinely asking about alcohol consumption and providing advice to pregnant women as well as identifying and supporting mothers ‘at risk of an alcohol-exposed pregnancy’ as early as possible.

Conclusions

This research aimed to increase the understanding of the antenatal advice given to expectant mothers about an important aspect of health in pregnancy. The study obtained data on midwives’ knowledge and attitudes about FASDs and how they chose to advise women about alcohol intake in pregnancy. Participating midwives clearly stated that they would like more information and support. More than a third had seen an infant with FAS, highlighting the need for more education in this area. It is essential that midwives feel better prepared to give appropriate advice so they can support women in making healthier choices for themselves and their babies.

Acknowledgments: Our thanks to all participating midwives and to the Addenbrooke's Charitable Trust for a grant to support the study costs.

.com/igflgmdm (accessed 1 February 2009)


Royal College of Midwives (2005) RCOG updates information on alcohol consumption. RCM, London


**FASD in Review**

March 2015


**Overall Summary**

Although FASD prevalence is now estimated to be higher than previously thought (May et al., 2014), challenges exist in obtaining access to diagnostic services in the United States due to an overall lack of awareness and diagnostic capacity (Astley & Grant, 2014). In addition, even if diagnostic resources are available in a given community, many providers do not have sufficient awareness about FASD to conduct screening that could lead to a diagnosis (Grant et al., 2013). When an individual does find diagnostic services, challenges still exist in obtaining an accurate diagnosis, for reasons including diagnostic challenges related to the breadth of the spectrum, cases of unknown maternal history of alcohol use, lack of consistent facial dysmorphism and growth impairment across diagnoses within the spectrum, and the high rate of co-occurring mental health disorders that can complicate differential diagnosis (Chasnoff et al., 2015; Greenbaum et al., 2009). These challenges have wide-ranging consequences, including a lack of appropriate early interventions, leading to ineffective services and poor outcomes (Olson et al., 2007).

**Diagnosis in Foster and Adopted Children with Prenatal Alcohol Exposure – Background**

Due to the diagnostic challenges with FASD, missed or misdiagnoses among individuals with an FASD can result in increased risk for secondary disabilities and co-occurring disorders. Risk also increases for abuse and trauma (Greenbaum et al., 2009; Henry et al., 2007), suicide (Huggins et al., 2008), and repeated involvement with the legal system (Streissguth et al., 2004; Streissguth et al., 1996). These risk factors are of particular concern in the foster care and adoption communities, as research has shown that the prevalence of FAS in foster care is 10 times higher (1/100) than in the general population (1/1000) (Astley et al., 2002). This new study by Chasnoff and colleagues adds to the evidence base on diagnostic issues for foster and adopted children with prenatal alcohol exposure.


This study examined the rate of misdiagnosis and missed diagnoses of FASD among a sample of foster and adopted children aged 4-18 referred to the Children’s Research Triangle (CRT), a children’s mental health center in Chicago, Illinois. CRT receives almost all of its referrals through the Illinois Department of Children and Family Services (DCFS), with the most common referral being behavioral problems. Approximately 30 percent of the children assessed each year at CRT receive an FASD diagnosis. All foster and adopted children aged 4-18 who have had a comprehensive evaluation completed at CRT were eligible for the study; a sample of 547 cases were pulled from approximately 3,000 charts of eligible clients.
Comprehensive evaluations at CRT include medical, mental health, and neurodevelopmental assessments. Medical assessments included a full pediatric, neurologic, and dysmorphology examination conducted by a board-certified pediatrician with extensive experience in FASD diagnosis and treatment. Prenatal exposure to alcohol is verified through documentation in birth records. Mental health assessments are conducted through a clinical interview with a licensed psychologist and a battery of instruments that assess child psychological and neurodevelopmental functioning.

All children are assigned an alcohol exposure-related diagnosis using the 4-digit code system developed by the University of Washington (Astley, 2006). Key definitions used to measure growth, dysmorphology, and neurodevelopmental features were specified:

- **Growth retardation:** Weight and/or height (past or current) less than the third percentile adjusted for age and gender (note: This is more restrictive than the 10th percentile recommended in the CDC guidelines (Bertrand et al., 2005), but recommended by Astley (Astley, 2006).
- **Facial dysmorphology:** Abnormal measurements of the upper lip and philtrum (rank 4 or 5) and shortened palpebral fissures, or after 2003, using the Lip-Philtrum Guide and the digital facial photograph based on criteria developed at the University of Washington (Astley & Clarren, 2001; Astley & Clarren, 2000).
- **Central nervous system abnormalities:** Documentation of microcephaly (head circumference below third percentile for age and gender and/or global cognitive delays demonstrated by performance below the third percentile on standardized testing or three or more domains of neurodevelopmental functioning more than two standard deviations below the normed mean on standardized measures of neurocognitive, self-regulatory, or adaptive functioning).

Diagnoses are given for Fetal Alcohol Syndrome (FAS) (deficits in all three criteria above); partial FAS (pFAS) (confirmed prenatal alcohol exposure plus facial dysmorphology and neurodevelopmental deficits); Alcohol-Related Birth Defects (ARBD) (confirmed prenatal alcohol exposure with major structural abnormalities only); and Alcohol-Related Neurodevelopmental Disorder (ARND) (confirmed prenatal alcohol exposure with neurodevelopmental deficits only). Pre- and post-assessments were analyzed using frequency tables, case summaries, and McNemar’s test for dependent proportions.

**New or Notable Information**

Descriptive data confirmed that all children in the sample (n=547) were in a foster or adoptive home at the time of referral and evaluation. Data were provided on mean age, gender, and racial distribution that were similar to the general distribution of children under the supervision of DCFS. Comparisons were provided for the diagnoses at referral and following the comprehensive evaluations. Key findings are summarized below.

<table>
<thead>
<tr>
<th>Prevalence of FASD within Sample</th>
<th>Of the reviewed group of 547 children, 156 were ultimately identified with a diagnosis related to prenatal alcohol exposure.*</th>
<th>Prevalence rate within sample = 28.52%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed Diagnoses of FASD</td>
<td>Of the 156 children identified with a diagnosis related to prenatal alcohol exposure, 125 had not been referred to CRT with such a diagnosis.</td>
<td>Missed diagnosis rate = 80.13% (125 out of 156)</td>
</tr>
<tr>
<td>Misdiagnoses of FASD</td>
<td>Of the 156 children identified with a diagnosis related to prenatal alcohol exposure, 10 had been referred to CRT with a different diagnosis within the spectrum.</td>
<td>Misdiagnosis rate = 6.41% (10 out of 156)</td>
</tr>
</tbody>
</table>

* FAS=93, ARND=61, pFAS=1, ARBD=1
Diagnoses Related to Mental Health:

- Referral: Most common diagnosis was for attention-deficit/hyperactivity disorder (ADHD).
- Post-Evaluation: Of the 156 children with a diagnosis of FASD, ADHD was still high (n=88), but 147 of those children received a co-occurring mental health diagnosis, with 104 having 2 or more mental health diagnoses. Diagnoses that were largely underdiagnosed included learning disorders, communication disorders, and intellectual disability, and objective signs of significant neurocognitive damage.

Implications of the New Research

The practical implications of this research are related to improving outcomes for foster and adopted children who have an FASD, as accurate diagnoses inform more appropriate interventions. For the 156 children diagnosed with FASD in this study, significant adjustments were made to the therapeutic approaches and medications prescribed. For example, increased needs for family therapy, sensory integration treatment, and psychotherapy were documented, as well as increased needs for further medical interventions, dental work, ophthalmology evaluations, attachment therapy, and educational services.

While the authors note that the study sample limits generalizability of the findings to the general population of children with an FASD, the findings nonetheless illustrate high prevalence of FASD in this sample of foster and adopted children, and high rates of missed diagnoses and misdiagnoses of both alcohol-related and mental health-related disorders. From a policy perspective, these findings have tremendous implications for provider awareness, diagnostic capacity, and treatment recommendations. Overall, providers need greater awareness about the risk of alcohol-related disorders in their treatment populations in order for proper screening to occur. Once screened, providers are in need of diagnostic services in order to obtain accurate diagnoses, which are then necessary for making appropriate treatment recommendations for those with an FASD.

These findings hold important implications for both policy and practice. Without increased awareness about the impacts of alcohol use during pregnancy, providers across service settings and target populations will miss the opportunity to improve treatment outcomes for their clients with an FASD. These missed opportunities lead not only to decreased quality of life for individuals with an FASD and their families, but also to increased burden and costs on the systems that may fail to respond appropriately to their clients who have an FASD. Based on recent research that suggests an increased prevalence of FASD (May et al., 2014), these implications warrant urgent attention to the training needs and lack of diagnostic capacity related to FASD that exist across the country.
References


