

Contents lists available at ScienceDirect

Genomics Data

journal homepage: www.elsevier.com/locate/gdata

Data in brief

Gene expression in the mouse brain following early pregnancy exposure to ethanol



Christine R. Zhang, Suyinn Chong*

Mater Research Institute – The University of Queensland, Translational Research Institute, Woolloongabba, QLD 4102, Australia

ARTICLE INFO

Article history:

Received 9 October 2016

Accepted 13 October 2016

Available online 19 October 2016

Keywords:

Gene expression
Hippocampus
Caudate putamen
Alcohol exposure

ABSTRACT

Exposure to alcohol during early embryonic or fetal development has been linked with a variety of adverse outcomes, the most common of which are structural and functional abnormalities of the central nervous system [1]. Behavioural and cognitive deficits reported in individuals exposed to alcohol *in utero* include intellectual impairment, learning and memory difficulties, diminished executive functioning, attention problems, poor motor function and hyperactivity [2]. The economic and social costs of these outcomes are substantial and profound [3,4]. Improvement of neurobehavioural outcomes following prenatal alcohol exposure requires greater understanding of the mechanisms of alcohol-induced damage to the brain. Here we use a mouse model of relatively moderate ethanol exposure early in pregnancy and profile gene expression in the hippocampus and caudate putamen of adult male offspring. The effects of offspring sex and age on ethanol-sensitive hippocampal gene expression were also examined. All array data are available at the Gene Expression Omnibus (GEO) repository under accession number GSE87736.

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Specifications

Organism/cell line/tissue	<i>Mus musculus</i> , C57BL/6J strain, hippocampus and caudate putamen at postnatal day (P)21 and/or P87
Sex	Male and female
Sequencer or array type	Illumina MouseWG-6 v2.0 Expression BeadChip
Data format	Raw and analyzed
Experimental factors	Prenatal ethanol exposure
Experimental features	Pregnant females were given free access to either 10% (v/v) ethanol or water from 0.5 days post coitum (fertilization) to 8.5 days post coitum. This window of exposure is equivalent, developmentally, to the first 3–4 weeks of gestation in humans, and models maternal alcohol consumption before pregnancy is confirmed. The peak maternal blood alcohol concentration is estimated to be 120 mg/dl or 0.12% [5]. Long-term effects on gene expression in the hippocampus and caudate putamen were examined in adult male progeny (n = 6 per group). The effects of offspring sex and age on ethanol-sensitive hippocampal gene expression were also investigated.
Consent	Animal work was conducted in accordance with the Australian code for the care and use of animals for scientific purposes, and was approved by Animal Ethics Committees at the Queensland Institute of Medical Research (P986, A0606-609M) and The University of Queensland (MMRI/120/12/NHMR).

(continued)

Specifications

Sample source location	C57BL/6J mice were obtained from the Animal Resources Centre, Perth, Australia
------------------------	--

1. Direct link to deposited data

<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE87736>

2. Experimental design, materials and methods

2.1. Prenatal ethanol exposure

Adult (6–8 week) C57BL/6J males and females were purchased from the Animal Resources Centre (Perth, Australia) and kept in individually vented cages on a 12-hour light/12-hour dark cycle with free access to standard chow (Irradiated rat and mouse diet, Specialty Feeds) for at least three days before mating. Mating pairs were left together continuously and females were checked each morning for the presence of a vaginal plug. When a plug was detected (designated 0.5 days post coitum) the male was removed from the cage and a bottle containing either 10% (v/v) ethanol or water was supplied to the female. The solutions were replaced daily and the volume of liquid (ml) consumed in the last 24 h was recorded. After 8 days of exposure, all females were provided with water until their litters were weaned. Only one

* Corresponding author.

E-mail address: suyinn.chong@mater.uq.edu.au (S. Chong).

cycle of ethanol exposure was performed per female. Offspring were weaned at postnatal day (P)21, after which male offspring were caged singly and female offspring were co-caged until tissue collection.

2.2. Tissue collection and preparation of total RNA

A total of six age- and sex-matched animals, from 3 to 5 litters, were analyzed per group (*i.e.* ethanol-exposed and controls). The hippocampus and caudate putamen were dissected from the same adult male animals at P87. For the caudate putamen, a brain blocker/slicer (Aster Industries, USA) was used to cut coronal sections at 1 mm intervals and tissue was collected from the fifth slice from the anterior end of the brain. The hippocampus was also collected from female offspring at P87 and male offspring at P21. Following dissection, tissues were immediately snap-frozen in liquid nitrogen and stored at -80°C .

Total RNA was prepared using the RNeasy Plus Mini Kit (Qiagen) according to the manufacturer's instructions. Tissues were homogenized in Buffer RLT Plus by passing 10 times through a 27-gauge needle attached to a sterile plastic syringe. RNA integrity and concentration were assayed using the Agilent 2100 Bioanalyzer system and RNA 6000 Nano Kit, following the manufacturer's instructions. All samples used for gene expression profiling had RNA integrity numbers (RINs) above 8.0.

2.3. Gene expression profiling on bead-based arrays and data analysis

Illumina's Direct Hybridization Assay and MouseWG-6 v2.0 Expression BeadChips were used to profile >45,200 transcripts per sample. For each sample, labeled complementary RNA (cRNA) was synthesized from 500 ng of total RNA using the TotalPrep RNA Amplification kit (Illumina) according to the manufacturer's instructions. The cRNA (1.5 μg per sample) was then hybridized to a MouseWG-6 v2.0 Expression BeadChip at 58°C for 16 h, according to the manufacturer's instructions. Each BeadChip was imaged using the BeadArray Reader iScan System (Illumina).

The sample probe profile was exported from GenomeStudio Gene Expression module (v1.9.0) into GeneSpring GX11 (Agilent) and analyzed for differential expression between groups. Briefly, the Biological Significance workflow was followed in which replicate samples were grouped and probesets were filtered by expression. Statistical analyses utilized the Mann-Whitney test (unpaired); *P*-value computation was set as "permutation" with a significance level of 0.05 and a fold change cut-off of 1.5. No genes passed multiple testing correction.

3. Results

Four genes were identified to be differentially expressed the adult (P87) male hippocampus in ethanol-exposed mice compared to

controls (fold change >1.5, uncorrected $P \leq 0.05$). The genes were *Indolethylamine N-methyltransferase (Inmt)*, *Melanoma inhibitory activity 1 (Mia1)*, *Solute carrier family 17 member 6 (Slc17a6)* and *Teashirt zinc finger family member 2 (Tshz2)*. Further filtering of the four genes involved removing any transcripts with low fluorescence intensity (≤ 500) and homology (BLAT) searches to confirm that the array probes were targeting the correct transcripts. Gene expression in the appropriate brain region was also checked using the Allen Brain Atlas [6]. After filtering, two candidate genes *Slc17a6* and *Tshz2* were selected for follow-up qRT-PCR experiments which confirmed ethanol-associated increased expression of *Slc17a6* in the adult male hippocampus [7]. No genes were found to be differentially expressed between groups in the P87 male caudate putamen, P87 female hippocampus or P21 male hippocampus, indicating that the effect of prenatal ethanol exposure on *Slc17a6* expression is tissue-, sex- and age-specific.

Acknowledgments

This work was supported by an Australian National Health and Medical Research Council grant (1003038) and an Australian Research Council Future Fellowship (FT100100333) to SC. CZ was supported by scholarships from The University of Queensland and Mater Research. This work was also supported by funding from the Mater Foundation (4509). The Translational Research Institute is supported by a grant from the Australian Government.

References

- [1] S.J. Astley, Profile of the first 1,400 patients receiving diagnostic evaluations for fetal alcohol spectrum disorder at the Washington State Fetal Alcohol Syndrome Diagnostic & Prevention Network. *Can. J. Clin. Pharmacol.* 17 (1) (2010) e132–e164.
- [2] S.N. Mattson, N. Crocker, T.T. Nguyen, Fetal alcohol spectrum disorders: neuropsychological and behavioral features. *Neuropsychol. Rev.* 21 (2) (2011) 81–101, <http://dx.doi.org/10.1007/s11065-011-9167-9>.
- [3] S. Popova, S. Lange, L. Burd, J. Rehm, Health care burden and cost associated with fetal alcohol syndrome: based on official Canadian data. *PLoS One* 7 (8) (2012), e43024, <http://dx.doi.org/10.1371/journal.pone.0043024>PONE-D-12-11269 (pii).
- [4] L. Ericson, L. Magnusson, B. Hovstadius, Societal costs of fetal alcohol syndrome in Sweden. *Eur. J. Health Econ.* (2016), <http://dx.doi.org/10.1007/s10198-016-0811-4>.
- [5] N. Kaminen-Ahola, A. Ahola, M. Maga, K.A. Mallitt, P. Fahey, T.C. Cox, et al., Maternal ethanol consumption alters the epigenotype and the phenotype of offspring in a mouse model. *PLoS Genet.* 6 (1) (2010), e1000811, <http://dx.doi.org/10.1371/journal.pgen.1000811>.
- [6] E.S. Lein, M.J. Hawrylycz, N. Ao, M. Ayres, A. Bensinger, A. Bernard, et al., Genome-wide atlas of gene expression in the adult mouse brain. *Nature* 445 (7124) (2007) 168–176, <http://dx.doi.org/10.1038/nature05453>.
- [7] C.R. Zhang, M.F. Ho, M.C. Vega, T.H. Burne, S. Chong, Prenatal ethanol exposure alters adult hippocampal VGLUT2 expression with concomitant changes in promoter DNA methylation, H3K4 trimethylation and miR-467b-5p levels. *Epigenetics Chromatin* 8 (40) (2015), <http://dx.doi.org/10.1186/s13072-015-0032-6>.