Report for the Alcohol Education and Research Council
on small grants' project:

The Epidemiology of Balance Problems in Childhood: the effect of alcohol consumption during pregnancy

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Introduction

Balance can be defined as the ability to maintain the body's centre of gravity over its base of support. This neurodevelopmental outcome underpins many motor skills such as the ability to stand, sit and walk and deficits in balance are thought to be associated with a variety of adverse psychosocial and educational outcomes in children. It is therefore important that risk factors for poor balance are investigated.

Despite Department of Health advice recommending that women should abstain from drinking alcohol during pregnancy (DoH, 2008), in the UK 8% of women continue to drink >2 units a week and 2% drink >7 units a week (The Information Centre, 2007). A recent systematic review looking at the effect of drinking alcohol during pregnancy on childhood balance (Humphriss et al, 2010) found limited evidence in this area, particularly for low to moderate levels of drinking. The present study therefore sought to explore this further using data from a UK-based birth cohort study.

Methods

The study group was taken from the Avon Longitudinal Study of Parents and Children (ALSPAC). ALSPAC is a birth cohort consisting of children born to pregnant women who were resident in the former Avon region of the UK and who

were due to give birth between April 1991 and December 1992 (n=14,541 giving rise to 13,988 live infants at 1 year). Further details of this study can be found on its website (www.bristol.ac.uk/alspac).

Prospective self-report measures of maternal total weekly alcohol consumption were available at the following stages of pregnancy: 8 weeks, 18 weeks, first 3 months, and 32 weeks. In addition, measures of maternal binge-drinking[1] at 18 weeks gestation, and maternal total weekly alcohol consumption pre-pregnancy[2] were available, as well as measures of paternal total weekly alcohol consumption and binge-drinking at 18 weeks gestation. Unlike many previous studies that have looked at the effect of alcohol exposure on neurodevelopmental outcomes and have deliberately selected for high levels of alcohol exposure, this study used "real-life" levels of alcohol consumption (predominantly low to moderate levels) as found with the ALSPAC parents.

Balance outcome data was available at ages 7 and 10 years. At age 7 a total of 5402 children completed a measure of dynamic balance using the heel-to-toe walking subtest of the Movement Assessment Battery for Children (mABC). At age 10, a total of 6915 children completed a variety of tests including dynamic balance (walking across a balance beam) and measures of static balance (standing heel-to-toe on a beam and standing on one leg) with both eyes open and eyes closed (see Humphriss et al, *in press,* copy included).

Data on a variety of potential confounding variables was also available. Measures of socioeconomic status included housing tenure, marital status, house crowding, maternal education, ethnicity and maternal social class. Measures of other drug use included smoking, cannabis and caffeine.

A series of logistic regression models were fitted to explore the effect of prenatal alcohol exposure on the 4 different balance outcomes. Maternal alcohol exposure was then substituted by paternal exposure in an attempt to determine whether the effects found could be explainable by an intrauterine mechanism.

[1] Defined as the number of occasions in the last month when at least 4 units of alcohol were consumed.
[2] Measured at 18 weeks gestation.

Finally, a maternal genotype, specifically the ADH1B gene for alcohol dehydrogenase, of which the rare dominant "A" allele is associated with lower levels of drinking in pregnancy (Zuccolo et al, 2009), was used as an instrumental variable to explore whether the effects found could be attributed to residual confounding. This methodology relies on Mendelian Randomisation giving the opportunity for a 'natural randomised control trial' in that genes are randomly distributed during meiosis. Unlike observational measures of alcohol consumption, Mendelian Randomisation means that a genotype such as ADH1B cannot be subject to confounding. The ADH1B genotype can therefore be used to substitute for observational measures of alcohol exposure without the need to adjust for confounders and without concerns about residual confounding.

Results

Logistic regression using the self-report measures of alcohol exposure revealed paradoxical findings in that alcohol was found to have a beneficial effect on balance ability, for several measures of exposure. These strong associations are presented in Table 1. None of the other associations between alcohol exposure and the balance outcome measures were found to be significant.

Table 1

A summary of the strong associations found between maternal alcohol exposure and balance outcomes

Balance outcome measure	**Maternal alcohol exposure at**	**Level of alcohol exposure**	**Adjusted[3] OR [95% CI]**
Dynamic balance, age 7	32 weeks	low	1.35 [1.08, 1.68]
SBEO, age 10	18 weeks	medium	1.23 [1.01, 1.49]
SBEC, age 10	8 weeks	low	1.23 [1.06, 1.43]
SBEC, age 10	18 weeks	medium	1.25 [1.06, 1.48]
SBEC, age 10	Binge-drinking, 18 weeks	high (>10 days/month)	1.67 [1.09, 2.58]

Key
SBEO = Static Balance Eyes Open summary measure
SBEC = Static Balance Eyes Closed summary measure
NB. OR>1 is indicative of better balance scores being more likely.

All analyses were then repeated substituting maternal for paternal measures of alcohol exposure. These analyses revealed several significant associations between some measures of paternal alcohol exposure and some of the balance outcome measures (see Table 2). It is therefore possible that some of the associations found in Table 1 might be the result of residual confounding, rather than the result of an intrauterine mechanism.

[3] Adjusted for confounders: marital status, crowding index, home ownership, parity, maternal education, ethnicity, maternal age, maternal social class, smoking, cannabis, caffeine (contemporaneous measures of maternal caffeine, cannabis and smoking exposure used as far as possible), number of maternal life events during pregnancy and maternal depression.

Table 2

Summary of strong associations found when using paternal alcohol exposure as a substitute for maternal consumption

Balance outcome measure	**Paternal alcohol exposure**	**Level of alcohol exposure**	**Adjusted OR [95% CI]**
Dynamic balance, age 7	Binge-drinking at 18 weeks	>10 days	1.39 [1.10, 1.76]
Dynamic balance, age 10	Pre-pregnancy	<1 glass/wk	0.49 [0.24, 0.97]
		≥1 glass/wk	0.47 [0.24, 0.91]
		≥1 glass/day	0.48 [0.24, 0.94]
Dynamic balance, age 10	First 3 months	<1 glass/wk	0.53 [0.30, 0.92]
		≥1 glass/wk	0.52 [0.30, 0.89]
		≥1 glass/day	0.50 [0.29, 0.88]
SBEO	First 3 months	<1 glass/wk	1.62 [1.10, 2.39]
		≥1 glass/wk	1.54 [1.06, 2.25]
		≥1 glass/day	1.65 [1.11, 2.44]

NB. OR>1 is indicative of better balance scores being more likely; OR<1 is indicative of better balance scores being less likely

To clarify this issue, the maternal ADH1B gene, rs1229984, was used as an instrumental variable to "deconfound" the analyses. The results of logistic regression analyses looking at the effect of the ADH1 gene on the 4 balance outcomes are given in Table 3. This analysis was restricted to subjects with "white" ethnicity, as having "non-white" ethnicity was found to be associated with having the rs1229984 gene (OR 6.20 [2.98, 12.91], p<0.0001).

Table 3

Associations between rs1229984 and balance outcome measures, in subjects with "white" ethnicity

Balance outcome measure	N	OR [95% CI]	P
Dynamic balance, age 7	3543	1.23 [0.91, 1.66]	0.1858
Dynamic balance, age 10	4132	1.04 [0.81, 1.33]	0.7519
SBEO	4148	1.12 [0.85, 1.48]	0.4238
SBEC	4162	1.16 [0.91, 1.49]	0.2289

No associations were found between ADH1B genotype and the balance outcome measures; having the rare "A" allele (which is associated with lower alcohol consumption) was not found to be associated with balance ability in childhood. Using the ADH1B gene as a "deconfounder" therefore enables us to conclude that that drinking alcohol during pregnancy did not have any effect balance on our balance outcome measures. The apparent beneficial effects of prenatal alcohol exposure found in Table 1 can be disregarded as being the result of residual confounding.

Conclusions

The main findings of this study are that drinking alcohol during pregnancy (at "real-life" levels) does not affect balance in children aged 7 and 10 years. Potential areas for further study include using measures of alcohol consumption recorded during the pre-pregnancy recognition period and using alternative measures of childhood balance.

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