COGNITIVE EFFECTS
A Systematic Review of Continuous Performance Task Research in Children Prenatally Exposed to Alcohol
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Abstract — Aims: The aim of this study was to review systematically, research investigating an association between the continuous performance task (CPT) in children and exposure to alcohol in utero, in order to identify any evidence of a specific deficit in performance.

Methods: Seven electronic databases and three websites were searched. Papers were selected in accordance with specific inclusion criteria and scored in terms of the methodological quality using the Newcastle–Ottawa score. Marked methodological heterogeneity limited the validity of any statistical meta-analysis and a descriptive synthesis was performed instead. Results: A total of 14 papers were identified for inclusion. There was no consistent evidence of any association between prenatal alcohol exposure and correct responses, reaction time, commission or omission errors during CPT testing. Apparent trends in the reported results, however, suggest that a potential effect might have been missed. Conclusions: Identifying a specific profile of CPT performance may assist in the detection and management of attention deficits amongst children with prenatal alcohol exposure. Future research with more consistent measures of exposure and outcome is, however, required before any valid generalizations about CPT performance can be made.

INTRODUCTION
Since Jones and Smith (1973) defined fetal alcohol syndrome (FAS), the effect of alcohol exposure in pregnancy has been widely debated. A number of impairments both physical and neuropsychological have been associated with exposure resulting in the description of several syndromes including, alcohol-related neurodevelopmental disorder (ARND), alcohol-related birth defects (ARBD), fetal alcohol effects (FAE) and partial fetal alcohol syndrome (PFAS) (BMA, 2007). These have been grouped collectively under the umbrella term, fetal alcohol spectrum disorder (FASD) (BMA, 2007). The incidence of FASD estimated from research in different geographical regions varies greatly. Although the rate in the UK is unknown, it is estimated that up to 9 in 1000 live deliveries in western countries are affected by FAS, PFAS or ARND (Autti-Rämö, 2002). The economic costs in terms of treatment, education, care and loss of productivity estimated in America in 2002 were $2 million (approximately £1.4 million) per individual affected (Lupton, 2003). Recent data suggest that alcohol consumption is increasing amongst women of child-bearing age in the UK (BMA, 2007), potentially increasing the population risk of this disorder. There is thus a need to develop our understanding of this important, costly and preventable condition.

Consistent evidence and hence clear diagnostic criteria for specific neuro-developmental deficits associated with intrauterine alcohol exposure are, however, limited (BMA, 2007). One of the most commonly described associations is that relating exposure to impaired attention. It is estimated that up to 60% of children with FASD may have deficits of attention, many of which are consequently diagnosed with ADHD (Mattson et al., 2006). This has sparked debate about the possibility of a similar aetiological pathway for these two disorders and/or the presence of overlapping symptoms. The continuous performance task (CPT) is one of the most frequently used, objective tools to measure sustained attention over time (Fried et al., 1992; Riccio et al., 2002). Impairments in performance have been documented amongst children with ADHD (Riccio et al., 2002), although they are less readily described amongst those with fetal alcohol exposure. The first CPT paradigm was designed by Rosvold et al. (1956). In the ‘X’ task, each subject tested is rapidly presented with a series of constantly changing, visual or auditory stimuli over a defined period of time, at a predetermined rate (Fried et al., 1992). They are instructed to respond when a particular stimulus, the letter X or an alternative ‘target stimulus’ is presented, but to withhold a response when any non-target stimulus is presented. Any target stimuli not responded to are recorded as omission errors whilst delayed or incorrect responses are recorded as commission errors (Riccio et al., 2002). Both are thought to reflect specific elements of attention deficit (Coles, 2001). In the ‘AX’ task, the target stimulus is modified such that participants are asked to respond only when the letter X or the alternative ‘target stimulus’ is immediately preceded by another specific stimulus, for example the letter A.

Two systematic reviews of CPT performance in children with ADHD have been conducted (Corkum and Siegel, 1993; Losier et al., 1996), but there are no similar reviews of CPT performance in those with fetal alcohol exposure of which we are aware. Individual studies suggest that children exposed to alcohol in utero exhibit deficits in performance, but the majority have small sample sizes and lack power to detect specific deficits. The use of the CPT as a diagnostic tool for ADHD has been considered in the past (Turkleson, 2000), although its sensitivity and specificity were found to be low. Indeed, a previous systematic review of CPT research (Riccio et al., 2002) concluded that whilst this test was sensitive to the presence of brain dysfunction, it was not useful in identifying specific underlying causes of brain damage. Detecting a deficit in performance amongst children prenatally exposed to alcohol may however highlight a potentially manageable dysfunction, directing more effective intervention for this important condition. We thus undertook a systematic review of available observational studies.
of CPT performance in children exposed to alcohol in utero to determine whether there is any evidence of such a deficit in performance.

**METHOD**

**Aim**
The aim of this systematic review was to identify the evidence for a specific, objective deficit of attention amongst children who had been exposed prenatally to alcohol.

**Search strategy**

A search strategy was constructed by one researcher with the assistance of a medical librarian. This incorporated key words and medical subject headings (‘MeSH terms’) for the population, the exposure, the timing of the exposure and the outcome. These were customized for each of the seven databases. The search was limited to include only human studies, written in the English language. The full strategy can be seen in the appendix.

The same strategy was used to search the grey literature, using SHOW (Scotland’s health on the web), NHS Scotland e-library and the UK department of health (DOH) websites.

**Selection of studies**
Studies were reviewed by the same researcher and included if they were original cohort, case-control or cross-sectional studies, published in a peer-reviewed journal. The title and abstract of each study included was used to determine its relevance to this review. A study was considered relevant if it investigated an association between prenatal alcohol exposure and attention amongst children between 0 and 18 years of age. Those studies identified were then read by the same researcher and reviewed against the following inclusion criteria.

**Exposure.** Only studies in which caregivers reported a history of prenatal alcohol exposure were included and not those that assumed this as a result of clinical features alone.

**Outcome.** Only studies that reported data regarding CPT performance were included. Since many variations of the CPT have been developed, we attempted to standardize the outcome measure by including only those that used an ‘X’, ‘AX’ or equivalent CPT paradigm in accordance with the original criteria of Rosvold et al. (1956). These specify that the task must involve the presentation of constantly changing stimuli with a clearly defined target stimulus.

The bibliographies of selected studies were also searched by hand in order to identify any further relevant studies not detected by the electronic search. No contact was made with the authors of any of the studies concerned.

**Assessment of quality**
The quality of each study was again assessed by one researcher, using the Newcastle–Ottawa Score (Wells et al.) and scored between 0 and 9. This is an instrument recommended by the

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**RESULTS**

**Study selection**
A flow chart outlining the selection process is presented in Fig. 1. Searches of the electronic databases identified a total of 352 studies. Of these, 60 studies were considered relevant and reviewed against inclusion criteria. A further 47 were excluded on the basis that they failed to use a continuous performance task (n = 44), failed to use an appropriate CPT paradigm (n = 2) or did not represent original research (n = 1). No further studies were yielded by searching the three websites of the grey literature.

Two additional studies were identified from hand searching the bibliographies of those selected. One of these was included
and the other excluded since the CPT paradigm was not as defined by Rosvold et al. (1956). This resulted in a total of 14 included studies.

**Description of included studies**

A summary of the main detail and outcomes of each of the 14 included studies is provided in Table 1. The studies were published across a 20-year period, ranging from 1996 to 2006. Of the 14 studies, 13 were conducted in the United States, 1 (Fried et al., 1992) being conducted in Canada. The majority of studies (9/14) selected children from hospital antenatal clinics with the remaining five selecting them from other research groups/specialist clinics. Sample sizes ranged from 40 in the study of Mattson et al. (2006) to 763 in the studies of Leech et al. (1999) and Richardson et al. (2002). Again, the majority included both boys and girls with only one considering boys alone (Suess et al., 1997). The age of children tested ranged from 3 to 16.9 years. This is important to consider since CPT performance appears to change with age. Evidence (Betts et al., 2006) suggests that there is continued improvement in the skill between 8 and 16 years, although the impact at younger ages is less certain. Many of the cited authors were involved in more than one of the included studies. These were largely independent, however, with the exception of the two studies written by Streissguth et al. (1986, 1994) and the two by Richardson et al. (2002) and Leech et al. (1999) that presented results for the same birth cohort examined at different ages. CPT performance amongst children prenatally exposed to alcohol formed the main experimental protocol in only 4 of the 14 studies.

There was marked methodological variability across the 14 selected studies in relation to the measurement of exposure and outcome. Whilst all 14 studies relied upon self-reported measures of exposure, a variety of quantitative and qualitative methods were used to define this. Eight studies quantified exposure, six of these using ounces of absolute alcohol (oz/AA) per day. Only half of these (Streissguth et al., 1986, 1994; Burden et al., 2005), however, state the conversion factor used to calculate oz/AA from the reported number of drinks consumed. Three of the studies (Suess et al., 1997; Lee et al., 2004; Mattson et al., 2006) combined self-reported measures with any documented detail of exposure following a review of medical, legal or social service records. The time at which exposure was measured also varied widely. Eight of the studies report measures of exposure relating to specific periods of pregnancy. Two of these (Streissguth et al., 1986, 1994) obtained measures in the fifth month of pregnancy, two (Leech et al., 1999; Richardson et al., 2002) at four- and seven-months gestation and at the time of delivery, two (Boyd et al., 1991; Burden et al., 2005) at each prenatal visit and two (Fried et al., 1992; Suess et al., 1997) in each trimester of pregnancy. The remainder of the studies did not specify a specific time to which the measurement of exposure was related.

Little detail was provided about individual parameters of the CPT paradigm despite evidence to suggest that there are a number of both internal and external parameters that affect performance (Riccio et al., 2002; Richardson et al., 2002; Betts et al., 2006). Only nine of the studies documented the length of time for which the children were tested with a CPT, which ranged from 6.3 min (Burden et al., 2005) to 90 min (Coles et al., 1997). Eight studies documented the proportion of stimuli presented during the CPT that represented the target stimulus and this varied from 10% (Richardson et al., 2002) to 75% (Lee et al., 2004). The duration for which a stimulus was displayed was reported in half of the studies and ranged from 50 to 300 ms. External parameters were even less consistently reported with only two studies mentioning the time of day at which testing was conducted and six failing to describe the instructions given to individual subjects prior to commencing testing.

Such marked variation limited the comparability of reported results and any meta-analysis was thus felt to be inappropriate. A descriptive synthesis of the available evidence was instead conducted.

**Methodological quality**

The scores for methodological quality ranged from 2 (Olson et al., 1998) to 8 (Streissguth et al., 1994). No formal sensitivity analysis was undertaken since no summary statistics were prepared.

Several of the studies and particularly those that compared inter-group differences were further limited by small sample sizes. The majority of the studies were also constrained by the extent to which they considered multiple outcomes, increasing the propensity for chance observations.

**Association of prenatal alcohol exposure and CPT performance**

Six of the 14 studies used some form of regression analysis to examine the association between prenatal alcohol exposure and CPT performance. Two of these (Streissguth et al., 1986, 1994) reported a significant association although only one (Streissguth et al., 1986) provided an estimate of the statistical significance. The remaining eight studies compared the performance between different exposure groups. Of these, six reported some differences in performance that were statistically significant.

Although those studies that compared inter-group differences in performance were more likely to report significant results, they were generally limited by smaller sample sizes and tended to be of lower methodological quality. The studies of Streissguth et al. (1986, 1994), Richardson et al. (2002) and Boyd et al. (1991) were most methodologically valid but provided contradictory evidence. Individual components of performance were thus considered in more detail in order to elicit any more consistent evidence of a specific deficit.

**Correct responses**

Of the 14 studies, 9 referred to some measure of correct response, 8 using it in their final analysis. Only two of these studies defined a correct response, however, Streissguth et al. (1986) describing it as a response within 1.4 s of a target stimulus and Boyd et al. (1991) as a response within 3 s. Burden et al. (2005) and Boyd et al. (1991) used regression analysis to investigate the relationship between exposure and the number of correct responses and reported no significant association. The remaining six studies considered inter-group differences, four of these reporting significant results. Whilst Mattson et al. (2006) and Brown et al. (1991) found those exposed to alcohol but without dysmorphic features of FAS were more accurate than those exposed to alcohol that exhibited dysmorphic features of
Table 1. A summary of the key details and findings from each of the 14 papers selected for review

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study design, population and setting</th>
<th>Quality score</th>
<th>Measurement of exposure</th>
<th>Outcome measures</th>
<th>Follow-up</th>
<th>Method of analysis and significant associations</th>
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</table>
| Streissguth et al. (1986) | 486 subjects selected from a consecutive cohort of attendees at two hospital prenatal clinics on the basis of self-reported alcohol and cigarette exposure in the prenatal period. Boys and girls 6.5–8.5 years | 7             | Structured interview in the 5th month pregnancy.  
- Average Oz AÂ/day  
- Binge score (average drinks per drinking occasion) | Visual ‘AX’ task: mean commission and omission errors/reaction time  
Visual ‘X’ task: mean commission and omission errors | 86% of original birth cohort followed up. Losses due to equipment failure/scheduling problems/lack of co-operation | Multiple regression examining the association of prenatal alcohol exposure and different components of CPT performance. Ounces AÂ/day was used as a measure of exposure in all instances except for the reaction time for which the binge score was used.  
‘X’ task: commission errors (0.40, P = 0.044), omission errors (0.27, P = 0.025) reaction time (0.38, P = 0.007)  
‘AX’ task: commission errors (0.45, P = 0.002), omission errors (0.32, P = 0.037) |  |
| Boyd et al. (1991)       | Prospective.  
359 subjects selected from a cohort of hospital prenatal clinic attendees.  
Boys and girls 4.8–5.0 years | 6             | Structured interview at each prenatal visit and postnatally.  
- Average OzÂ/day in pregnancy | Visual modified ‘X’ task using pictures. Mean number of correct and incorrect responses and mean reaction time | Incomplete follow-up of cohort. Losses due to lack of co-operation/distant move/loss of contact/medical illness/gross mental retardation/late data collection/equipment failure/unavailability | Multivariate regression. No significant association between average exposure in oz AÂ/day and any CPT parameter |  |
68 subjects selected from a longitudinal cohort of hospital clinic attendees, on the basis of exposure to alcohol in the prenatal period. Boys and girls 5–8 years | 5             | Post-natal questionnaire.  
Groups categorized as  
- never drank  
- stopped drinking in the 2nd trimester  
- drank throughout pregnancy | Visual modified ‘X’ task using numbers. Mean number of correct responses/omission and commission errors. | No description of any loss to follow-up. | MANOVA/MANCOVA  
Those exposed throughout pregnancy made significantly fewer correct responses than other exposure categories with more omission and commission errors. This became non-sig when adjusted for current maternal alcohol use T-test. No significant differences in CPT performance for exposed and non-exposed groups |  |
| Fried et al. (1992)      | Prospective.  
140 exposed and 50 non-exposed subjects voluntarily self-referred.  
Boys and girls 6 years | 5             | Structured interview in each trimester.  
- Oz AÂ/day (cut-off >0.14) | Visual modified ‘AX’ task using single digit numbers. Mean number of correct responses/omission and commission errors. | 63 lost to follow-up | T-test. No significant differences in CPT performance for exposed and non-exposed groups |  |
| Streissguth et al. (1994) | Prospective.  
500 subjects selected from a consecutive cohort of attendees at two hospital prenatal clinics on the basis of self-reported alcohol and cigarette exposure in the prenatal period. Boys and girls 13.9–15.7 years | 8             | Structured interview in 5th month pregnancy.  
- Oz AÂ/day  
- Average no. of drinking occasions per month  
- Binge score (Â≥5 drinks on any one occasion)  
- Max. no. of drinks on any one occasion  
- Average no. of drinks on any one occasion  
- Average daily and massed drinking score  
- Overall summary score | Visual ‘X’ and ’AX’ tasks.  
Mean number of commission and omission errors/reaction time/standard deviation of reaction time | 82% of original cohort followed up. No explanation of losses | Partial least squares analysis examining the relationship between a composite score or prenatal alcohol exposure and different components of CPT performance. Coefficients:  
’X’ task: Commission errors = 0.09, omission errors = 0.06, reaction time = 0.12, standard deviation of reaction time = 0.27.  
‘AX’ task: Commission errors = 0.19, omission errors = 0.10, reaction time = 0.05, standard deviation of reaction time = 0.20 |  |

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Table 1. Continued

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<tr>
<td>Coles et al. (1997)</td>
<td>Prospective. 122 children selected on the basis of age from a longitudinal study of the effects of prenatal exposure. 27 children matched for age and socio-economic status referred from an ADHD clinic. Boys and girls 7.0–8.5 years</td>
<td>5</td>
<td>Structured interview  Groups categorized as - exposed/dysmorphic (FASD, n = 25) - exposed/not dysmorphic (EtOH, n = 62) - not exposed/normal (CON, n = 35) - not exposed/ADHD (ADHD, n = 27)</td>
<td>Visual task, no details given. Mean number of hits/number of false alarms/reaction time/standard deviation of reaction time</td>
<td>52% of FASD group, 25% of EtOH group, 43% of CON group and 60% of ADHD group lost to follow-up. No explanation provided</td>
<td>ANOVA Significant difference in the mean number of hits: FASD = 150, EtOH = 163, CON = 143, ADHD = 106 (P &lt; 0.04)</td>
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<td>Suess et al. (1997)</td>
<td>Retrospective. 43 subjects selected from methadone clinic/volunteers. Boys only 7–12 years</td>
<td>4</td>
<td>Telephone or face-to-face interview with examination of medical records. Groups categorized as - exposure to alcohol (ALC) - exposure to opiates (OP) - exposure to opiates and alcohol (ALC/OP) - no exposure in pregnancy (NON)</td>
<td>Visual modified ‘AX’ task using numbers. Mean percentile score for correct responses and commission errors</td>
<td>Complete follow-up</td>
<td>ANOVA Significant difference in the number of commission errors: ALC = 57%, OP = 59%, ALC/OP = 92%, NON = 50% (P &lt; 0.01) Post hoc analysis: ALC/OP made sig. more commission errors than ALC (P &lt; 0.05) or NON (P &lt; 0.01)</td>
</tr>
<tr>
<td>Olson et al. (1998)</td>
<td>Retrospective. FAS and non-exposed groups consecutively selected from subsets of the ‘Fetal Alcohol Follow-Up study’ and the ‘Seattle Longitudinal Prospective Study’ respectively. Boys and girls 14–16 years</td>
<td>2</td>
<td>Self-reported exposure. Groups categorized as - dysmorphological features of FAS (n = 9) - light/no exposure to alcohol in the prenatal period (n = 174)</td>
<td>Visual ‘X’ and ‘AX’ tasks. Median number of commission errors, mean reaction time and standard deviation of reaction time</td>
<td>No description of any loss to follow-up</td>
<td>Wilcoxon two sample rank sum. No significant differences in performance between the FAS group and the comparison group</td>
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<tr>
<td>Leech et al. (1999)</td>
<td>Prospective. 763 subjects, selected from a consecutive cohort of attendees at a hospital prenatal clinic, on the basis of alcohol or marijuana consumption in the prenatal period. Boys and girls 5.5–8.9 years</td>
<td>7</td>
<td>Structured interview at 4 and 7 months gestation and at delivery. Groups categorized as - exposed (≥3 drinks/week 1st trimester) - not exposed (≥3 drinks/week 1st trimester)</td>
<td>Visual modified ‘X’ task using coloured shapes. Mean number of omission and commission errors</td>
<td>88% of original cohort followed up. Losses due to refusal of child/maternal time constraint/change of address/deceased/handicap/colour-blindness/incomplete assessment</td>
<td>Stepwise multiple regression. No significant association between prenatal alcohol exposure and CPT performance</td>
</tr>
<tr>
<td>Richardson et al. (2002)</td>
<td>Prospective. 763 subjects, selected from a consecutive cohort of attendees at a hospital prenatal clinic, on the basis of alcohol or marijuana consumption in the prenatal period. Boys and girls 10–13 years</td>
<td>7</td>
<td>Structured interview at 4/5 and 7 months gestation and 24–48 hr post delivery. Groups categorized as - Light exposure (&lt;0.4 drinks/day) - Moderate exposure (0.4–0.89 drinks/day) - Heavy exposure (&gt;0.89 drinks/day)</td>
<td>Visual modified ‘AX’ task. Mean omission and commission errors</td>
<td>145 lost to follow-up. Losses due to change of address (n = 46)/untraceable (n = 3)/refused participation (n = 40)/failure to complete tests (n = 23)/testing detrimental to subject (n = 3)</td>
<td>Stepwise multiple regression. No significant association between prenatal alcohol exposure and CPT performance</td>
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<tr>
<td>Coles et al. (2002)</td>
<td>Prospective. 181 subjects recruited consecutively between 1980–1985, from a prenatal hospital clinic, 84 volunteers from a school board, matched for a number of demographic criteria. Boys and girls 13–17 years</td>
<td>5</td>
<td>Self report Groups defined as - exposed/dysmorphic (DYSM $n = 46$) - exposed/not dysmorphic (EtOH $n = 82$) - not exposed/normal’ (CON $n = 53$) - not exposed/special education (SED $n = 84$)</td>
<td>Visual modified ‘X’ and ‘AX’ tasks and auditory task. Mean number of hits/omission and commission errors/delay to respond</td>
<td>Complete follow-up</td>
<td>ANOVA. Significant differences in: Mean no. hits (visual) DYSM = 28.96, EtOH = 32.16, CON = 30.91, SED = 29.68, ($P &lt; 0.003$) Bonferroni comparison: DYSM and SED made fewer correct responses than EtOH. Mean commission (visual) DYSM = 8.18, EtOH = 4.69, CON = 4.61, SED = 5.72 ($P &lt; 0.04$) Bonferroni comparison: DYSM made more errors than any other group. Mean omissions (visual) DYSM = 7.13, EtOH = 3.84, CON = 4.95, SED = 6.31 ($P &lt; 0.003$) Bonferroni comparison: DYSM and SED made fewer correct responses than EtOH.</td>
</tr>
<tr>
<td>Lee et al. (2004)</td>
<td>Retrospective. 30 alcohol-exposed children from a neuropsychological research project referred by themselves, health or social service professionals. 30 non-exposed children self-referred in response to community outreach or advertising. Boys and girls 9.0–16.9 years</td>
<td>4</td>
<td>Self-reported exposure with examination of medical/social records. Groups categorized as - heavy exposure (ALC, $n = 30$) - light/no exposure (CON, $n = 30$)</td>
<td>Visual modified ‘X’ task using shapes. Mean number of commission and omission errors</td>
<td>No description of any loss to follow-up</td>
<td>ANOVA. Significant differences in: Commission errors: ALC = 81.9, CON = 95.1 ($P = 0.010$). Omission errors: ALC = 66.1, CON = 86.5 ($P = 0.028$)</td>
</tr>
<tr>
<td>Burden et al. (2005)</td>
<td>Prospective 480 subjects selected consecutively from 1986–1989 from a hospital prenatal clinic. Boys and girls 7.2–8.9 years</td>
<td>6</td>
<td>Structured interview at each prenatal visit. - Average oz AA/day (cut-off 0.5)</td>
<td>Visual ‘X’ and ‘AX’ task. Mean % of correct hits/ commission errors/mean reaction time/standard deviation of reaction time</td>
<td>143 subjects not followed up. No explanation provided</td>
<td>Multiple regression. No significant association between prenatal alcohol exposure and CPT performance</td>
</tr>
<tr>
<td>Mattson et al. (2006)</td>
<td>Retrospective. 20 alcohol exposed children from families interested in participating and referred by health professionals. 20 children recruited in response to advertisement in the community or volunteered from families of staff members. Boys and girls 9–14 years</td>
<td>5</td>
<td>Structured interview and examination of medical/legal/social records. Groups categorized as - heavy exposure (FASD, $n = 20$) - light/no exposure (CON, $n = 20$)</td>
<td>Visual modified ‘X’ task using shapes. Auditory modified ‘X’ task using high or low tones. Mean % correct hits/mean no. of false alarms/mean reaction time</td>
<td>14 exclusions due to matching criteria. 4 subjects unable to complete task</td>
<td>ANOVA. Significant differences in: Correct responses: FASD = 94%, CON = 98% ($P &lt; 0.001$). Reaction time: Visual: FASD = 480–500 ms, CON = 440–450 ms ($P &lt; 0.01$) Auditory: FASD = 550–670 ms, CON = 540–590 ms ($P &lt; 0.01$)</td>
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FAS (1997) or those from a special education or ADHD group (2002). Since these four studies were less methodologically valid than those of Burden et al. (2005) and Boyd et al. (1991), it could not be concluded that there was any balance of evidence to suggest an overall effect of exposure on the number of correct responses made.

**Commission errors**

Of the 14 studies, 13 referred to some form of commission error, although only five attempted to define this, one (Leech et al., 1999) defining it as ‘an incorrect response’, one (Coles et al., 2002) as ‘an inability to inhibit a response’, one (Olson et al., 1998) as ‘a false alarm’ and two (Richardson et al., 2002; Lee et al., 2004) as ‘a response to a non-target’. Five of these studies analysed the association between exposure and commission errors using regression analysis with only two (Streissguth et al., 1986, 1994) reporting a significant relationship. Of the remaining eight studies that compared inter-group differences, three reported significant results (Brown et al., 1991; Coles et al., 2002; Lee et al., 2004). Although again there was no consistent evidence of any overall significant effect, trends in the reported data suggest that there may indeed be a real effect of exposure that has been missed, with four (Fried et al., 1992; Coles et al., 1997; Suess et al., 1997; Olson et al., 1998) of the studies reporting non-significant results demonstrating that those exposed made more commission errors on average than those not exposed. This must be considered in future research.

**Omission errors**

Eight of the studies measured some form of omission error, five (Brown et al., 1991; Fried et al., 1992; Leech et al., 1999; Richardson et al., 2002; Coles et al., 2002) defining it as a missed target, one (Lee et al., 2004) as a lack of correct response and two (Streissguth et al., 1986, 1994) providing no definition. Four of these studies compared inter-group differences, with three (Brown et al., 1991; Coles et al., 2002; Lee et al., 2004) reporting a significant difference. Supporting evidence from the more methodologically valid studies was, however, again inconsistent, two (Streissguth et al., 1986, 1994) reporting a significant association between prenatal alcohol exposure and the number of omission errors, and two (Leech et al., 1999; Richardson et al., 2002) reporting no significant association. As for commission errors, there was an apparent trend in the reported results, all four of the studies comparing inter-group differences demonstrating a greater number of errors in those exposed when compared with those not exposed.

**Reaction time**

Eight studies considered the reaction time during the CPT although none attempted to define this. Four studies (Streissguth et al., 1986, 1994; Boyd et al., 1991; Burden et al., 2005) used regression analysis to examine the association between exposure and reaction time, with two of these (Boyd et al., 1991; Burden et al., 2005) reporting no significant association. The remaining four studies (Coles et al., 1997, 2002; Olson et al., 1998; Mattson et al., 2006) compared inter-group differences in this parameter, only one (Mattson et al., 2006) reporting any significant effect. Despite this, three of the studies (Olson et al., 1998; Coles et al., 2002; Mattson et al., 2006) demonstrated that exposed individuals were on average slower to react, a trend that again suggests a potential real, but undetected, effect.

**Auditory performance**

Only two studies (Coles et al., 2002; Mattson et al., 2006) considered auditory CPT performance and both considered relatively small sample sizes. Mattson et al. (2006) reported that reaction time was significantly longer in those exposed prenatally to alcohol, whilst Coles et al. (2002) reported no significant difference in the reaction time amongst different exposure groups. With limited evidence from only two studies, it is difficult to draw any valid conclusion about the association of exposure with auditory performance.

**DISCUSSION**

In summary, this review demonstrates that, in the current literature, no specific component of CPT performance in children has consistently been found to be associated with prenatal alcohol exposure. This does not mean that there is no effect of prenatal alcohol exposure on CPT performance and apparent trends in the reported results suggest that a real effect may have been missed. This has potentially important implications for child development, since deficits of attention may affect virtually all purposeful behaviours.

If, as the trends in this review suggest, children exposed to alcohol make more commission and omission errors than those not exposed, their behaviour is similar to that described in the review of CPT performance in children with ADHD conducted by Losier et al. (1996). A more detailed comparative analysis of performance might, however, reveal more specific and subtle differences between these two groups with implications for appropriate management. Furthermore, it may prove possible to distinguish other diagnostic groups with similar presenting features on the basis of performance.

Current evidence of the effects of prenatal alcohol exposure on behaviour suggests that any postulated association between the two is complex. Although the exact underlying relationship is as yet uncertain, it appears likely that it is influenced by both the time and size of exposure (Riley and McGee, 2005). Furthermore, it has been suggested that a number of other factors, including those correlated with maternal drinking during pregnancy and the post-natal environment (D’Onofrio et al., 2007) are associated with observed effects. Indeed, a third study published by Streissguth et al. (1995) found that collectively, covariates accounted for a larger fraction of the variation in CPT performance across their cohort than pre-natal alcohol exposure itself. It thus remains difficult to separate any potential direct or indirect aetiological effects of prenatal exposure from those of other variables influencing behaviour. Further studies with larger sample sizes are likely to be required to address this issue. Similarly, objectively identifying behavioural disorders represents a challenge to researchers, with many diagnoses such as ADHD relying upon observations or reports from parents and teachers (O’Malley and Nanson, 2002). Inferences from adult opinion about a child’s behaviour may not always be accurate, however (Landeman-Dwyer and Ragozin, 1981), and behavioural scales are not designed to delineate more complex underlying cognitive mechanisms of behaviours such as attention (Losier et al., 1996). The CPT may thus provide a more
appropriate objective tool to further investigate these complexities amongst children with fetal alcohol exposure.

The marked methodological heterogeneity that may explain some of the inconsistency in reported outcomes in this review has also been described in other reviews of CPT performance (Corkum and Siegel, 1993; Losier et al., 1996) and by those reviewing the effects of prenatal alcohol exposure (Henderson et al., 2007). This emphasizes the need for further consistent and more detailed research before any valid generalizations can be made.

Limitations
Several methodological limitations should be considered when interpreting the results of this review. Firstly, the articles in this study were only reviewed by one researcher, limiting the validity with which they were included or excluded. The specific nature of the inclusion and exclusion criteria made the selection of studies relatively straightforward. There were, however, occasional difficulties in determining the nature of the CPT protocol employed, the resolution of which may have benefited from the involvement of a second researcher. Included articles were also limited to those that were available in the English language. Although the Newcastle–Ottawa score is a valid instrument to assess the methodological quality, it is limited by the methodological detail that each study provides. It cannot necessarily be assumed that what has not been reported has not been done. In addition, this score does not consider many of the issues pertinent to aetiological studies of teratogenicity, such as the timing or frequency of measurements of exposure. The data extraction, analysis and assessment of quality were again conducted by only one researcher increasing the propensity for bias and possible under- or overestimation of the findings described. Of the studies, 14 were conducted in the United States and some caution should thus also be exercised when extrapolating the findings to other countries, since factors such as the pattern of drinking and the propensity to report alcohol consumption in pregnancy may vary. Finally, as with any systematic review, there is the possibility of publication bias. In our study, however, such bias seems unlikely, since both positive and negative associations between prenatal alcohol exposure and CPT performance were identified.

CONCLUSION
This is the only systematic review of CPT performance in children exposed prenatally to alcohol as far as we are aware. Despite its limitations, it offers a comprehensive review of the current evidence base including attempts to access the grey literature. In future, more consistent, comparative studies are, however, required before any valid generalizations can be made. These should be directed in particular towards

- identification of a specific measure of prenatal alcohol exposure, incorporating pattern, timing, duration and consistent conversion measures,
- the construction of an optimal CPT protocol considering both internal and external task variables and
- detailed, comparative studies of children with prenatal alcohol exposure, children with ADHD and children with both ADHD and prenatal alcohol exposure, in order to elicit any subtle differences in performance.

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APPENDIX


Population
(child or children or childhood or infant$ or adolescent$ or juvenile$ or youth).mp. [mp = title, original title, abstract, name of substance word, subject heading word]
OR “School Child”/
OR “Infants”/
OR adolescent/ or child/ or child, preschool/ or infant/
OR adolescent/ or juvenile/ or child/ or preschool child/ or school child/ or toddler/ or infant/
OR adolescents/ or children/ or youth/

Exposure
(prenatal or gestational or foetal or fetal or foetus).mp.
[mp = title, original title, abstract, name of substance word, subject heading word]
OR antenatal.mp. [mp = title, original title, abstract, name of substance word, subject heading word]
OR “Prenatal Period”/
OR “Prenatal Influences”/
OR “Prenatal Exposure”/
OR pregnancy/ or maternal–fetal exchange/
OR “Fetus”/
OR “Expectant Mothers”/
OR prenatal injuries/ or prenatal exposure delayed effects/
OR Maternal Exposure/
AND alcohol$.mp. [mp = title, original title, abstract, name of substance word, subject heading word]
OR “Alcohol”/
OR “Alcohol Consumption”/
OR “Alcohol Drinking Patterns”/
OR “Alcohol Abuse”/
OR alcohols/ or ethanol/
OR drinking behavior/ or alcohol drinking/
OR alcohol-related disorders/ or alcohol-induced disorders/ or alcoholic intoxication/ or alcoholism/
OR prenatal alcohol.mp. [mp = title, original title, abstract, name of substance word, subject heading word]
OR “Fetal Alcohol Syndrome”/

Outcome
“Impulsive Behavior”/
OR “Hyperactivity”/
OR “Attention”/
OR “Attention Deficit Disorder”/
OR (Sustained attention or vigilance).mp. [mp = title, original title, abstract, name of substance word, subject heading word]
OR “Attention Deficit Hyperactivity Disorder”/
OR “Attention Deficit Disorders”/
OR attention deficit and disruptive behavior disorders’/ or attention deficit with hyperactivity/
OR attention deficit disorder or disruptive behavior/
OR attention deficit disorder with hyperactivity/ or attention deficit disorder/ or attention span/ or distractibility/ or impulsiveness/ or oppositional defiant disorder/
OR Conduct disorder.mp. [mp = title, original title, abstract, name of substance word, subject heading word]
OR (Continuous performance task or CPT).mp. [mp = title, original title, abstract, name of substance word, subject heading word]
OR (adhd or AD or attention deficit or hyperactiv$).mp. [mp = title, original title, abstract, name of substance word, subject heading word]

Searches for population exposure and outcome were combined using AND, before removing duplicates, limiting to English and then to human [mp = title, original title, abstract, name of substance word, subject heading word].

REFERENCES