A critical review of “Relation of Prenatal Alcohol Exposure to Cognitive Processing Speed and Efficiency in Childhood”

Recently a growing body of literature has shown that individuals affected by fetal alcohol spectrum disorder (FASD) show deficits in executive function (EF). Executive function is a broad term used to describe a wide range of cognitive processes based in the frontal lobe involving deliberate actions such as planning, strategizing, inhibition, set-shifting, flexible thinking, and most critically, working memory (WM). Working memory is believed to be a particularly important component of EF, and individuals with FASD have shown deficits in tasks designed to assess WM. The authors of the current study believe that the observed WM deficits are mediated by deficits in cognitive processing speed. Their hypothesis is based on several studies demonstrating that fetal-alcohol affected individuals show greater retention times, or fixation times, in various cognitive tasks, thereby indicating slower processing speed.

The objective of the current study was to determine the degree to which processing speed deficits are found in later childhood in relation to prenatal alcohol exposure where mothers drank moderate-to-heavy levels of alcohol during pregnancy. The sample consisted of 337 black children from the Detroit Prenatal Alcohol Longitudinal Cohort, assessed at 7.5 years of age (interquartile range, 7.5 to 7.9). Mothers were recruited during their first prenatal visit between September 1986 and April 1989 from a large urban maternity hospital clinic in Detroit. Mothers were recruited to over-represent moderate-to-heavy drinking by including all women who reported alcohol consumption at conception averaging at least 0.5 oz absolute alcohol (AA) per day (about one standard drink). A random sample of approximately 5% of the lower level drinkers and abstainers were also invited to participate, and to reduce the risk of alcohol being confounded by cocaine, 52 heavy cocaine, light alcohol, users were also included in the samples. Alcohol drinking history was taken at each prenatal visit and averaged across clinic visits to provide “oz AA per day during pregnancy”. Detailed drug use histories were also obtained each visit except the first.

The children were assessed using the Sternberg paradigm for the original Sternberg memory scanning test, memory rotation test, number comparison test, and arrow discrimination test, all of which depend on working memory function but with respect to different cognitive domains. For example, the memory rotation test is designed to assess visuospatial working memory, while the number comparison and arrow discrimination tasks assess magnitude estimation in working memory. Briefly, the Sternberg paradigm relies on the following principles. An item is presented, followed by a delay, and then another item (which may or may not be the original item) is re-presented for the participant to recognize as either previously seen or not previously seen. The time it takes for the participant to respond, the retention time (RT), is representative of the time it takes the subject to perceive the object, encode its identity, scan short-term memory, decide on the response, and to respond. This is used to assess working memory, and in the current study, processing speed of the above processes. The number of items originally presented varies in order to vary the difficulty of the task (memory load). The RT is expected to increase with task difficulty and is thought to represent the additional time needed to process the added information. This can be depicted as a graph of RT versus memory load, with the intercept representing the time it took to respond when only one item was presented, signifying the
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“overall processing speed” of the task, and the slope representing “processing efficiency” as memory load (task difficulty or item numbers) is increased. The children were also tested on the colour naming portion of the Stroop Color-Word test, which involves relatively “automatic processing”, in order to compare the relation of prenatal alcohol exposure to RT of “effortful cognitive processing” in contrast to that of “automatic processing”.

At first glance, one may suspect the homogeneity of the sample, which shares low socioeconomic status among other confounding variables, to be problematic in the analysis of the data. However, hierarchical linear modeling (HLM) was most appropriately chosen for the data analysis in order to account for any potential confounders. The group analyzed a broad list of confounders that included 23 variables under the categories: demographics, other prenatal exposures, child-rearing environment, current drug/alcohol use by primary giver, situational variables, and postnatal lead exposure. Any variable that was even slightly correlated to overall RT (p < 0.10) was included in the HLM analysis. Hierarchical linear modeling has the advantage of more accurately modeling true relationships between outcomes (such as retention time) and predictors (such as prenatal alcohol exposure) because it allows for multilevel analysis of multilevel data, incorporating the effects of potential confounders by modeling cross-level interactions, particularly among homogenous data.12

The investigators of the study report evidence of slower overall RT in relation to prenatal alcohol exposure for metal rotation, arrow discrimination, and memory scan tasks, and a fetal alcohol-related effect on processing efficiency of the number comparison task. A significant relation between prenatal alcohol exposure and “overall processing speed” (signified by the intercept of RT versus memory load graph) was found for the arrow discrimination task (p < 0.010); an almost significant relation was found between prenatal alcohol exposure and “overall processing speed” for the mental rotation, and the memory scan tasks, (p = 0.063, and p = 0.098, respectively); a significant relation was found between prenatal alcohol exposure and “processing efficiency” (signified by the slope of RT versus memory load graph) for the number comparison task; and no significant relation was found between prenatal alcohol exposure and Stroop color naming task.

Based on the above results, the investigators concluded that slower processing speed was evident in school-aged children exposed to moderate-heavy levels of alcohol prenatally, but only on tasks requiring some cognitive effort.

The authors conclude that the data confirms a link between prenatal alcohol exposure and slower processing speeds, and that this deficit is found within the context of complex cognition and not automatic processing. However, if the authors are discussing trends that failed to reach conventional levels of statistical significance, they fail to mention the almost significant association between maternal depression during pregnancy and “processing efficiency” for the arrow discrimination task (p = 0.074).

Given, the rather large sample size, and the detailed modeling of confounders, it is noteworthy that not all the associations reported achieved conventional levels of statistical significance. It is possible that due to the rigorous nature of the analysis an even larger sample size is necessary to distinguish such associations in such heavily nested data. Alternatively, 84% of the sample’s mothers reported drinking during pregnancy, with 73% reporting a mean of 2.6 standard drinks of alcohol a day. Also, it is possible that those mothers considered “abstainers” were not necessarily true abstainers and might have underreported their drinking for fear of stigmatization. This overrepresentation of alcohol-exposed children could have obscured or minimized cognitive deficits, if present, because of the lack of a large and true control group being modeled into the HLM analysis. Additionally, prenatal exposure was modeled as AA/day. There is evidence that there may be a threshold type effect regarding prenatal alcohol exposure and cognitive deficits, where doses of ethanol per occasion (binge drinking) may be more relevant to cognitive outcomes than averaged overall doses throughout pregnancy.5 If this relation is true, the current modeling of the study would also help to obscure relationships between prenatal alcohol exposure and cognitive deficits. Furthermore, it has been reported13 that not all heavily exposed fetuses may have detectible deficits, perhaps due
to pharmacokinetic or genotypic differences, however this may be an artifact due to the methodological difficulties associated with employing strategies to study ethanol dose response relationships in the human fetus, as well as epidemiology of fetal alcohol exposure.

The current study had good construct validity in the four Sternberg tasks measured because RT did increase within each task as the level of difficulty increased. Also, the investigators felt confident that the relation shown between prenatal alcohol exposure and slower processing speed (although not always significant) was not an artifact of slower performance due to errors because the error rates were quite low (ranging 11-23%) and did not correlate with prenatal ethanol exposure. This fact is encouraging because it shows that deficits in processing speed were not likely mediated by IQ, because tasks mediated by IQ are associated most often with error rates, and that the data are consistent with previous studies that show fetal-alcohol exposed individuals have marked WM deficits greater than predicted by their IQ.²

Lastly, the current study reports a path analysis that shows a significant correlation between prenatal alcohol exposure and processing speed ($\beta = 0.13$), between prenatal alcohol exposure and working memory ($\beta = -0.15$), and between processing speed and working memory ($\beta = -0.26$). The authors conclude that the results of the path analysis supports their hypothesis that the prenatal alcohol effect on working memory was in part mediated by the associated deficit in processing speed. Although, the path analysis results are consistent with the investigators hypothesis, the authors fail to mention that the path analysis cannot confirm a causal relationship, especially when noting that two of the four main associations they found were not statistically significant (the relationship between prenatal ethanol exposure and processing speed in the memory scanning, and mental rotation tasks). Furthermore, the authors insist that the slower RT intercepts are indicative of slower processing speed in prenatally alcohol-exposed children without discussion of other possible explanations such as the use of different processing strategies.¹¹

In conclusion, the current study made an excellent attempt at controlling for possible confounders in a heavily nested set of data, and did find evidence suggestive of possible slower processing speeds in specific cognitive tasks among children exposed to alcohol prenatally. It is important to remember that the cognitive steps taken to resolve the tasks are process-specific, and therefore generalizations made from isolated tasks in certain cognitive domains should be made with caution. Therefore, the studies claim that the data confirms a link between prenatal alcohol exposure and slower processing speeds, and that this deficit is found within the context of complex cognition and not automatic processing, is too broad a statement given the amount of evidence.

REFERENCES
10. Burden MJ, Jacobson SW, Jacobson JL. Relation of prenatal alcohol exposure to cognitive...
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