Prenatal drug exposure alters adolescent neural responses in a probabilistic reward/punishment task

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AIM

To assess the impact of prenatal drug exposure on adolescent decision making in the face of variable uncertainty and reward.

INTRODUCTION

- Prenatal drug exposure has been associated with cognitive and affective deficits, including difficulties with emotional regulation (Ackerman et al 2010), likely related to processing of rewards and punishments.
- Animal models suggest prenatal drug exposure causes structural and molecular changes relevant to reward functioning as well as changes in behavioral expressions of reward functioning (Malanga et al 2003, Gendle et al 2003, Lidow 2003).
- The Wheel of Fortune task (Ernst et al. 2004) involves choosing between two different monetary outcomes with different probabilities. The task probes willingness to take risks versus preference for safer choices as well as responses to differing levels of uncertainty.

METHODS

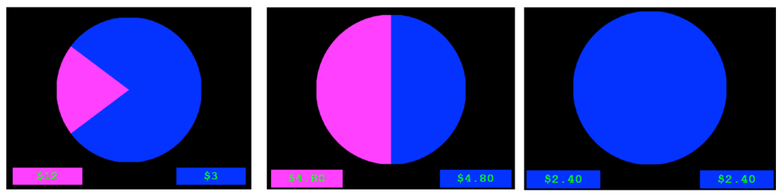
Subjects: 39 African-American adolescents

- Twenty-two exposed to drugs in utero (primarily cocaine but also some alcohol, cigarettes, opiates and marijuana)
  - 10 male, 12 female
  - 14.23 +/- 1.06 years old
  - 21/22 right-handed
- Seventeen non-exposed from same neighborhood and socioeconomic status
  - 5 male, 12 female
  - 13.59 +/- 1.27 years old
  - 17/17 right-handed
- All were enrolled in an ongoing longitudinal follow up study at University of Maryland, Baltimore School of Medicine of infants exposed to drugs in utero.

Task: Wheel of Fortune

- Modified so that all choices had the same expected value and differed only in certainty of outcome (See Figure 1).
- Eight blocks of 20 trials each
- Alternated between 'Win' and 'Loss' blocks
- 40 80/20% wheels, 20 100% wheels 20 50/50% wheels presented in 'Win' blocks. Same breakdown for 'Loss' blocks.
- Participants were able to keep up to $50 of their final total

Choice phase



Outcome phase

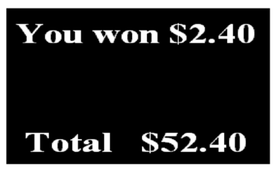


Figure 1: Wheel of Fortune task: Sample of wheels from 'Win' block. Wheels counterbalanced for color and side were also employed. The same wheels were also used in 'Loss' blocks. All wheels had the same expected value of $2.40.

Imaging:

- Siemens Allegra 3T scanner
- Acquisition parameters: TE/TR = 27/2000 ms, FA = 77°, and a voxel size of 3.44´3.44´4 mm^3.
- High-resolution T1-weighted anatomical images were acquired for registration purpose.

Analysis:

- Focused on the choice phase of the task.
- Analysis done in AFNI using 3dMEMA
- Maps of activation to each type of stimulus (win100%, win50%, win80%(chose 80% side of 80/20% wheel), win20%(chose 20% side of 80/20% wheel), and corresponding lose conditions were generated for the group as a whole and for the exposed and control groups separately.
- Contrast maps of the different wheel types were generated for:
  - win100% vs win50% to look at the effect of uncertainty
  - win100% vs win80/20%(chose 20%) to look at making a riskier choice
  - win100% vs win80/20%(chose 80%) to look at making a safer choice
  - win50/50% vs win80/20%(chose 80%) to look at active choice for more certainty compared to choice of no consequence for certainty of outcome
  - win50/50% vs win80/20%(chose 20%) to look at active choice for higher risk reward compared to choice of no consequence for certainty of outcome
  - Corresponding contrasts for loss wheels
- Direct comparison of maps for the two groups were used to assess the effect of PDE on task activation.

RESULTS

Subjects:

- Matched on gender, age and non-maternal care
- Differed on exposure to alcohol and cigarettes in utero

Behavior:

- All participants responded slower to 'Loss' wheels than to 'Win' wheels and used response 1 (key under index finger) more frequently than response 2 (key under middle finger). Exposed group used response 1 significantly more than non-exposed group.
- Exposed participants were slower when making any 20% choice ('Win' or 'Loss' wheels) and slower when choosing on an 80/20% wheel in the 'Loss' blocks (regardless of choice made).
- Wide variety in choice on 80/20% wheels but no difference by group (See Figure 2).

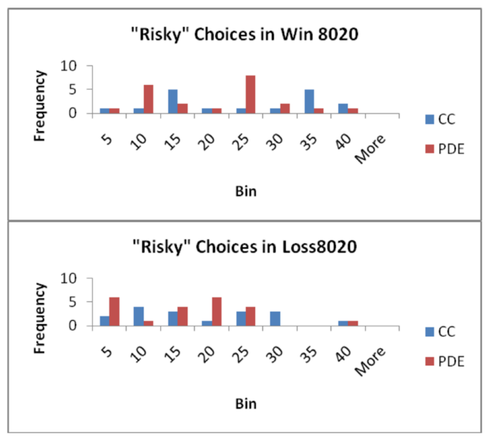


Figure 2: Frequency histogram of risky choice (20% side of wheel) during 'Win' and 'Loss' blocks by group. No significant difference in choice by group.

Imaging:

- **Task maps:** All 8 choice types (Win100, Win50/50, Win80/20sel20, Win80/20sel80 and corresponding Loss choices) produced very similar maps with activation in medial frontal/anterior cingulate, striatal regions, fronto-parietal attention network, insula and visual cortex (See Figure 3).

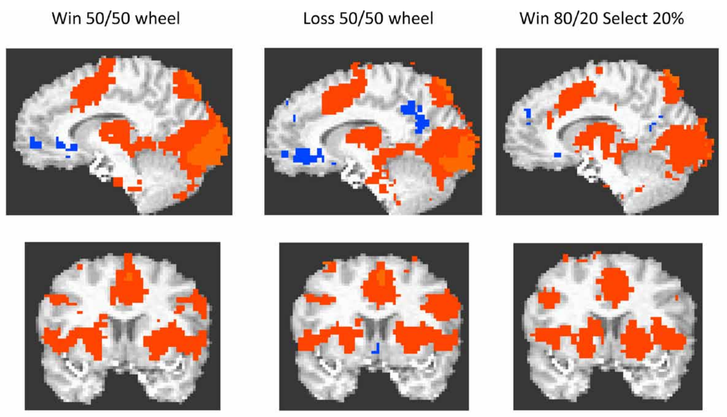


Figure 3: Task maps: Representative maps showing the activation that was similar across all decision types. (x=10, y=-8, z=30, voxel-wise p<0.001, corrected to p<0.05, right=left)

- **Contrasts between task maps:** Few contrasts yielded significant differences between activation related to the various choices. Figure 4 shows significant differences in Win100 vs Win80/20 (select 20% side) and Loss 100 vs Loss80/20 (Select 20% side).

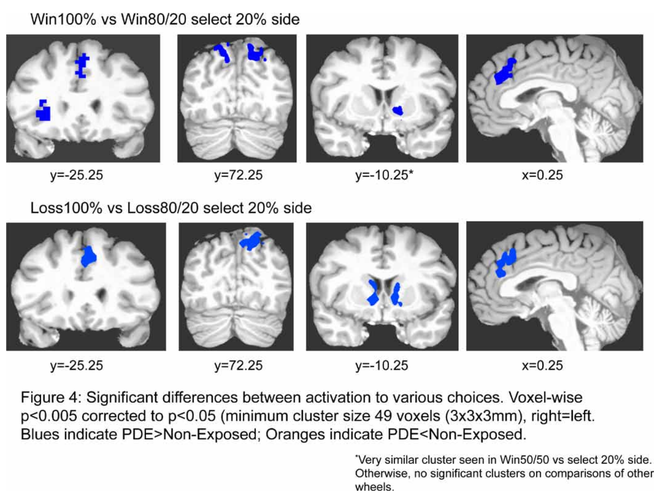


Figure 4: Significant differences between activation to various choices. Voxel-wise p<0.005 corrected to p<0.05 (minimum cluster size 49 voxels (3x3x3mm), right=left. Blues indicate PDE>Non-Exposed; Oranges indicate PDE<Non-Exposed.

*Very similar cluster seen in Win50/50 vs select 20% side. Otherwise, no significant clusters on comparisons of other wheels.

- **Contrasts between groups:** All significant differences between groups were found in contrasts of task maps between groups and maps were similar.
  - Mostly driven by activation in the exposed group's map that was absent in the control group's map.
  - Regions showing this pattern were largely posterior (middle occipital gyrus, cuneus, precuneus, lingual gyrus, fusiform gyrus and some posterior parietal and temporal regions) but also included precentral gyrus, right inferior frontal gyrus/BA 44 and medial frontal/cingulate. (See Figures 5 and 6)

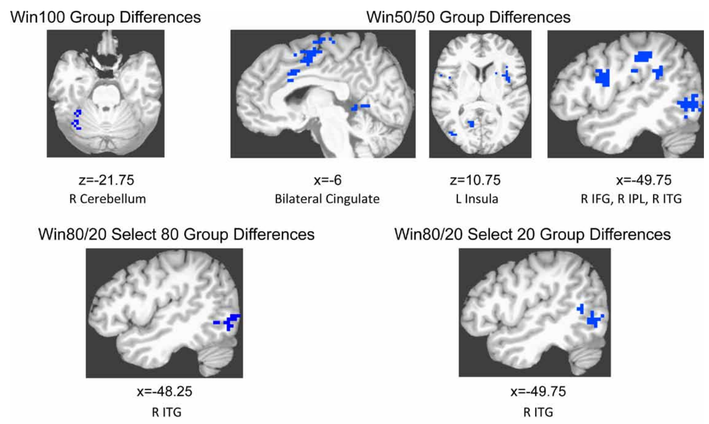


Figure 5: Between group differences during choices on Win wheels. Voxel-wise p<0.005 corrected to p<0.05, right=left. Blues indicate PDE>Non-Exposed; Oranges indicate PDE<Non-Exposed.

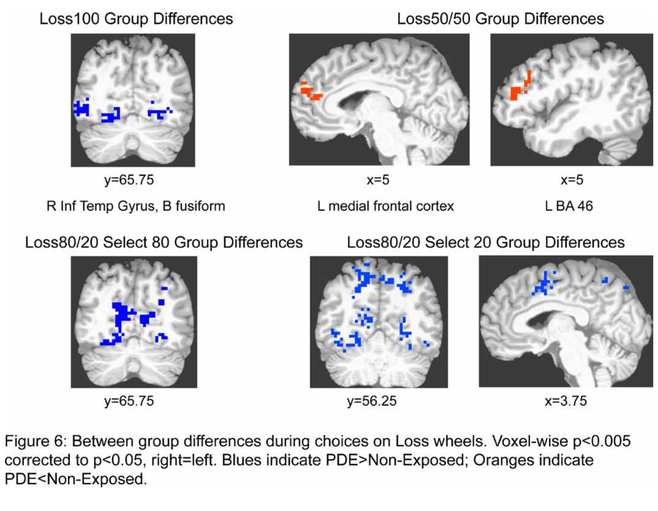


Figure 6: Between group differences during choices on Loss wheels. Voxel-wise p<0.005 corrected to p<0.05, right=left. Blues indicate PDE>Non-Exposed; Oranges indicate PDE<Non-Exposed.

CONCLUSIONS

- Making a risky choice engages attention and reward areas in adolescents.
- Adolescents exposed to drugs in utero show increased activation in response to a probabilistic stimulus predictive of reward and punishment in numerous areas associated with attention and response to probabilistic reward valuation (Peters 2009). This increased activation during a variety of choices combined with slower reaction times may reflect less efficient processing as a consequence of prenatal drug exposure.
- Adolescents exposed to drugs in utero show reduced activation in frontal regions associated with executive control when required to make a choice based on chance alone in the context of an impending loss.

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