

# Effects of HIV exposure and gender on VMI scores and neurometabolite levels at 5 and 7 years

## Study

Neuropsychological testing was performed and single voxel <sup>1</sup>H-MRS (SVS) data were acquired in the midfrontal gray matter (MFGM) and the peritrigonal white matter (PWM) on a Siemens 3T Allegra Head Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa on a cohort of HIV uninfected children (HIV exposed (HEU) and HIV unexposed (HUU)) at ages 5 and 7. MRS data were acquired with a real-time motion and B<sub>0</sub> corrected [1] point resolved spectroscopy (PRESS) sequence (TR 2000 ms, TE 30 ms, 64 averages, Scan Time: 2:16 min). Water reference scans were acquired for eddy current compensation, frequency/phase correction, and to compute absolute metabolite levels. Spectra were analysed with LCModel. Statistical analyses performed in R. A mixed effect linear regression model was used to account for repeated measures.

**Subjects:** We obtained both neuropsychological and MRS data: in the MFGM on nineteen 5-year old (10 female; mean age ± standard deviation = 5.4 ± 0.4 years; 13 Xhosa/6 Cape Coloured; 12 HEU/7 HUU) and twenty-five 7-year old children (8 female; 7.3 ± 0.1 years; 18 Xhosa/7 Cape Coloured; 8 HEU/17 HUU), with eleven children imaged at both ages. In the PWM on twenty-three 5-year old (11 female; 5.5 ± 0.4 years; 14 Xhosa/9 Cape Coloured; 14 HEU/9 HUU) and twenty-eight 7-year old children (9 female; 7.3 ± 0.1 years; 22 Xhosa/6 Cape Coloured; 10 HEU/18 HUU), with ten children imaged at both ages. All HEU children were exposed to treatment for prevention of mother-to-child transmission (PMTCT).

## Background

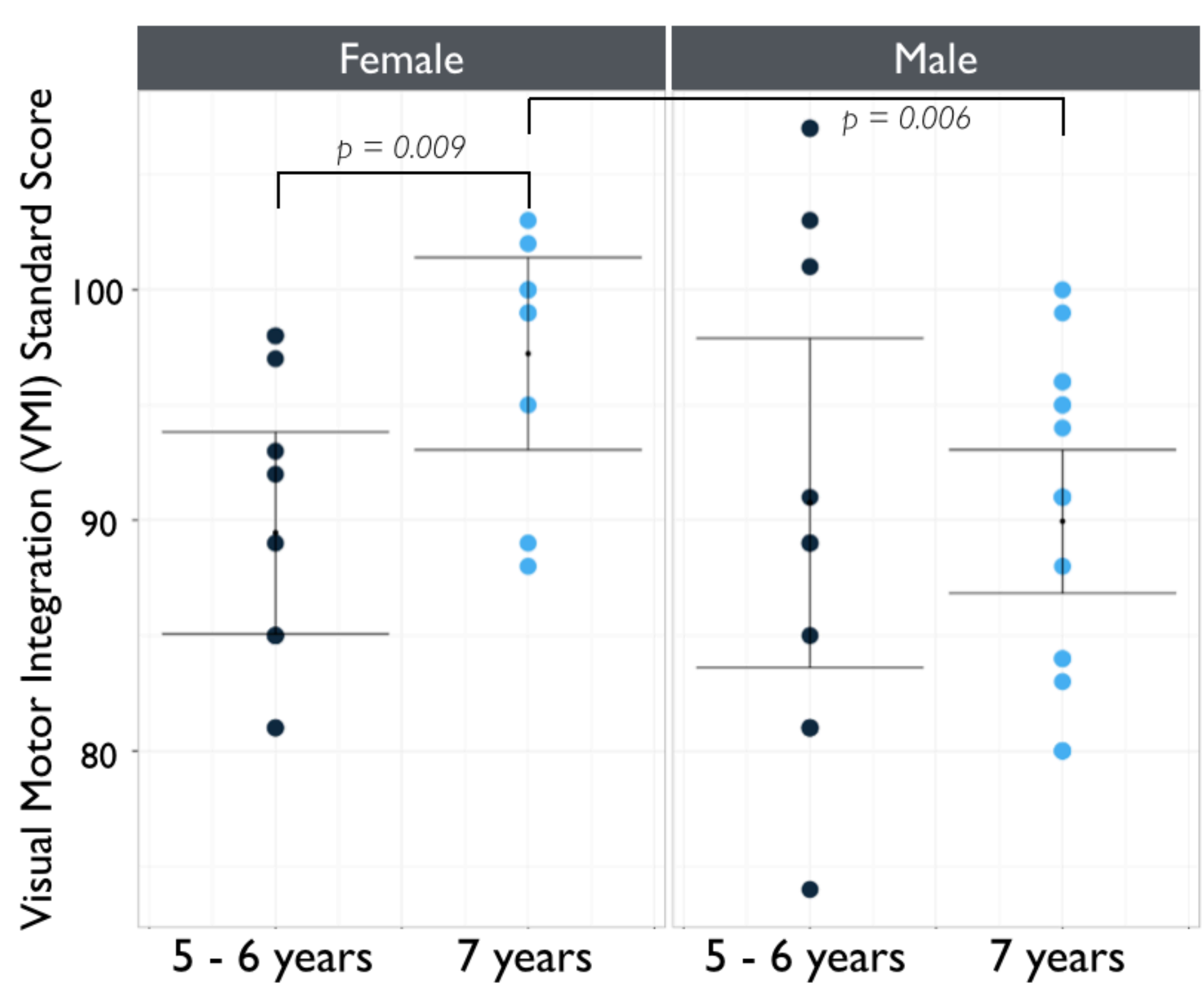
In South Africa, 95% of HIV-positive pregnant women and 68% of HIV-exposed infants have been receiving antiretroviral therapy (ART) [2,3]. Several studies [4,5,6,7] suggest that *in utero* ART exposure is associated with long-term neurological effects - such as cognitive delay and motor abnormalities - motivating additional study of HIV-exposed uninfected (HEU) children. The increased risks may involve exposure to HIV antibodies, antiretroviral (ARV) drugs and environmental factors [8].

MR spectroscopy (MRS) is used for the non-invasive investigation of neurological development in children. Choline is associated with cellular density [9]. Creatine is related to energy metabolism, and found in neurons and glia [9]. Both metabolites remain constant in childhood [10]. Metabolite levels often correlate with neuropsychological measures [10,11]. The Beery-Buktenica Developmental Test of Visual-Motor Integration (VMI) provides a measure of the ability to integrate visual perception and motor abilities [12].

**We explored perinatal HIV exposure and gender effects on the relationship between metabolite levels and VMI measures over a 2-year period in children.**

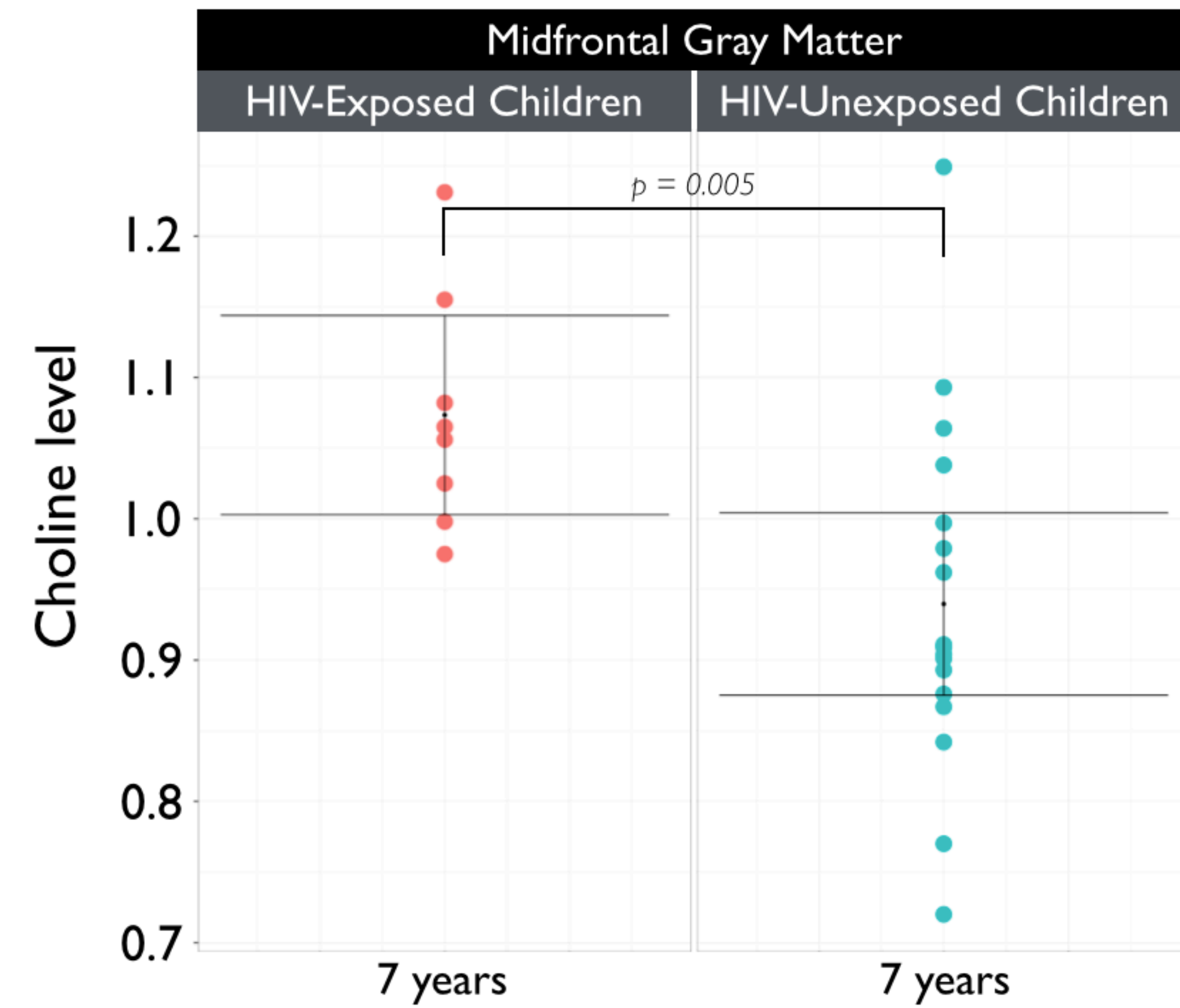
## Results

### 1 Girls have HIGHER mean VMI scores at age 7



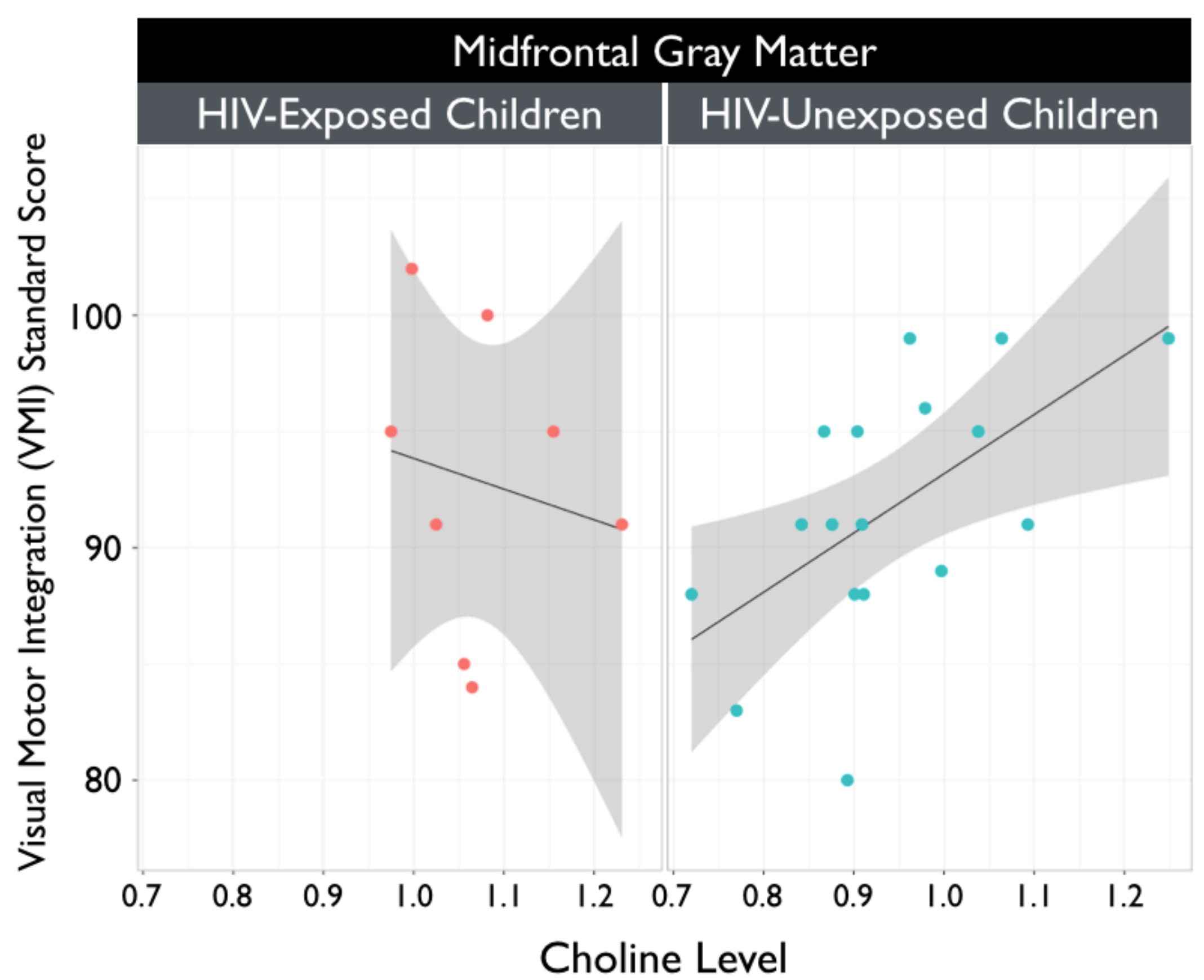
**Result:** We find increased visual motor integration (VMI) standard scores from age 5 to 7 among girls *only* (VMI: 89 ± 7 vs 97 ± 5;  $p = 0.009$ ). At age 7, girls have higher mean VMI scores than boys ( $p = 0.006$ ). Bars represent confidence intervals.  
**Interpretation:** The significant gender differences at age 7 suggests developmental differences in visual perception and motor abilities; at school age, girls may develop these abilities earlier than boys.

### 2 HEU children have HIGHER mean choline levels in MFGM at age 7



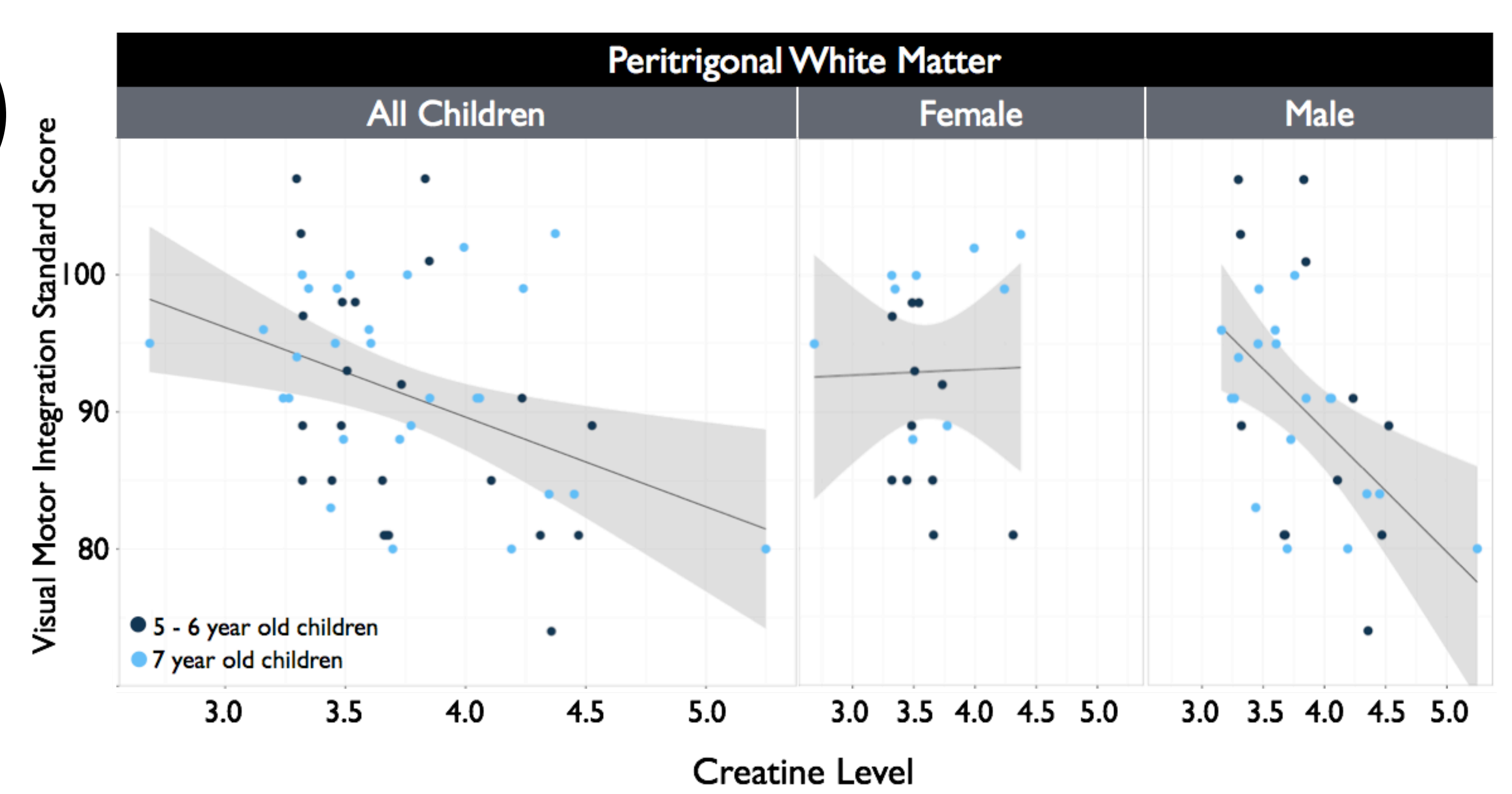
**Result:** In MFGM, HEU children have HIGHER mean choline levels at age 7 compared to HUU children (cho (HEU) = 1.07 ± 0.8, cho (HUU) = 0.94 ± 0.13;  $p = 0.005$ ).  
**Interpretation:** The increased mean choline levels among HEU children compared to HUU children suggest developmental differences among HEU children. Increased choline levels may imply glial proliferation/inflammation or increased cellular density.

### 3 At age 7, VMI scores correlate with choline levels in MFGM in HUU children only



**Result:** In the MFGM, we found a significant positive correlation between VMI scores and choline levels in HUU children at age 7 ( $p = 0.01$ ).  
**Interpretation:** The positive relationship between VMI scores and choline levels among HUU children *only* may be related to the difference in mean choline levels between HEU and HUU children (result 2). The relationship is independent of gender, despite observed gender difference in VMI scores (result 1). The positive correlation between VMI scores and choline levels in HUU children at age 7 suggest the relationship is a possible indicator of healthy neurological growth.

### 4 At age 5 and 7, VMI scores correlate with creatine levels in PWM in boys only



**Result:** We found a negative correlation between VMI standard scores and creatine levels in the PWM in all children (slope = -6.5,  $p = 0.02$ ) at ages 5 and 7. Based on gender, the relationship is *only* significant among male children ( $p = 0.01$ ) across both ages.  
**Interpretation:** Our results suggest metabolite levels may provide additional insight into the evolution of cognitive measures during childhood, as well as possible differences based on gender.

## References

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