Associations Between Hippocampal Volume and Cognitive Function in Children with Chromosome 22q11.2 Deletion Syndrome

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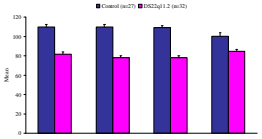
INTRODUCTION

- Chromosome 22q11.2 deletion syndrome (DS22q11.2) occurs in 1-2:4000 live births as the result of a a 1.5 - 3Mb deletion on chromosome 22 (Murphy & Scambler, 2005).
- Syndrome is characterized by:
  - Intelligence scores in "borderline" range (typically PIQ > VIQ)
    - Impaired spatial memory, visuospatial attention, numerical and temporal cognition
  - Increased risk for developmental psychopathology (e.g., ADHD, OCD, Schiz)
- Reduced gray and white matter in parietal regions & medial cerebellum consistently reported (e.g., Eliez et al., 2000; Simon et al., 2005)
- Goal of the present investigation was to assess abnormalities of the amygdala and hippocampus in 7- to 14-year-old children with DS22q11.2 and explore associations with cognitive phenotype.

PARTICIPANTS

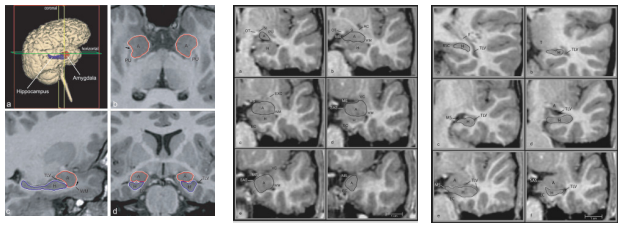
A total of 72 children (ages 7-14 years) participated

- 36 children FISH positive for chromosome 22q11.2 deletion
  Mean = 10 years 9 months (± 2 yr 4 mo)
  19 female, 17 male
- 36 age-matched typically developing controls
  Mean = 10 years 6 months (± 1 yr 11 mo)
  13 female, 23 male



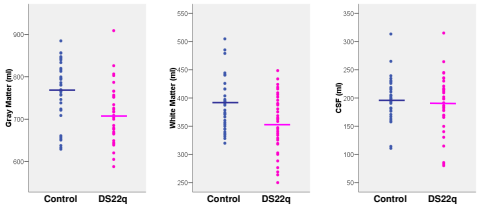
METHODS

- Data were acquired at 3 scanner sites using a 1.5T Siemens Vision and 2 3T Siemens Trios
  - For each subject, a three-dimensional high-resolution (1mm isotropic) structural MRI was acquired using a T1-weighted MP-RAGE sequence.
  - **Although data collection site was not correlated with any of the volumetric measurements it was entered as a covariate in all analyses.**
- Total brain volume (gray/white matter and CSF) was calculated using SPM2.
- Neuroanatomical guidelines were used to define borders of the amygdala and hippocampus bilaterally and volumes were calculated based on manual tracings of the regions (see Schumann et al., 2004 for details of procedure).



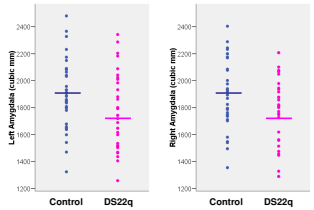
RESULTS - TOTAL BRAIN TISSUE

- DS22q11.2 had significantly less gray and white matter compared to controls.
  - 2 Group x 3 Region MANCOVA w/ site and age entered as covariates, $Fs(1, 68) = 10.12, 8.6$, $ps<.01$
- CSF volume did not differ between the groups ($p>.49$).



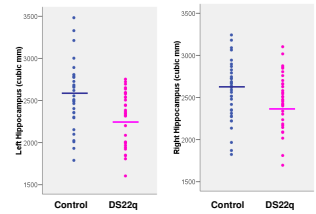
RESULTS - AMYGDALA

- No significant group differences in bilateral volumes of the amygdalae after controlling for differences in gray matter.
  - 2 Group x 2 Hemisphere MANCOVA w/ gray matter, site, and age entered as covariates $ps>.15$



RESULTS - HIPPOCAMPUS

- Left hippocampal volume was significantly reduced in children with DS22q11.2, even after controlling for differences in gray matter.
  - 2 Group x 2 Hemisphere MANCOVA w/ gray matter, site, and age entered as covariates
    Left Hippocampus: $F(1, 65) = 7.29$, $p<.01$; Right Hippocampus: $p>.60$



Note: Analyses of amygdalae and hippocampi volumes excluded two outliers to ensure that the necessary criteria were met for employing parametric statistics (normality and homogeneity of variance).

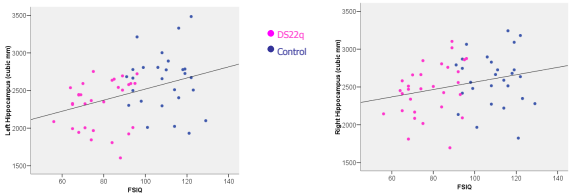
ASSOCIATIONS WITH COGNITION

- Hippocampal volume was significantly correlated with performance on standardized measures of cognition. All correlations between IQ and hippocampal volume remained statistically significant after entering age, gray matter, and data collection site as covariates.

Results of correlational analyses between brain structures and IQ measures

	Full Scale IQ n = 57	Performance IQ n = 57	Verbal IQ n = 57	Processing Speed n = 52
Gray Matter	.17	.23	.20	.02
White Matter	.15	.22	.19	-.08
CSF	-.03	.11	-.01	**-.27***
Left Amygdala	.14	.20	.17	-.05
Right Amygdala	.14	.18	.15	-.03
Left Hippocampus	**.37****	**.44****	**.38****	.14
Right Hippocampus	**.27****	**.38****	**.30****	.03

*p<.05, **p<.01



SUMMARY

- Children with DS22q11.2 exhibited smaller left hippocampal volumes compared to age matched controls
- Children with DS22q11.2 also exhibited smaller volumes of the right hippocampus, and amygdala bilaterally, but not disproportionately to reductions in gray matter.
- This study is the first to show associations between decreased hippocampal volume and cognition in DS22q11.2 (similar to reports in typically developing children: Schumann et al., 2007).
  - After controlling for differences in gray matter, significant correlations were observed between hippocamapal volume and IQ
  - Amygdalae volumes were not related to cognitive assessments
- Given the known association between memory impairment, risk for psychosis, and reduced hippocampal volume (Lawrie et al., 2002; Wood et al., 2003) careful characterization of hippocampal morphology and associations with cognition *in the same participants* are essential for predicting outcomes in individuals with this syndrome and for the understanding of neurodevelopmental disorders in general.

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