A previous publication (Walsh et al 2008) had reported an increased rate of rare gene interrupting CNVs relative to an adult population and to controls. However since that time, many schizophrenia related CNVs have been reported and their pleiotropic influence has been marked.

We have examined the rates of disease related CNVs including replicated CNVs for autism, ID, epilepsy and schizophrenia (Ahn et al 2013). Using the 1M and 2.5 M Illumina chips, stringent CNVs that passed all QC filters (≥100 kb size, ≥1 gene) were considered disease related if they were within the CNV loci or had greater than 50% overlapping with reported in large (sample size of cases >300) association studies with schizophrenia, Autism Spectrum Disorder (ASD), intellectual disability (ID) or epilepsy. Based on 25 large case-control studies, our final list includes 48 candidate loci.

Our present data are for a total of 126 COS probands 69 having a healthy full sibling who have been screened for these 48 loci, 11.9% of COS probands (15 out of 126) have rare disease-associated CNVs higher than the estimated 5.1% seen in adult onset cases (Ahn et al 2013); 5 (4%) of 126 COS probands have a 2.5-3Mb 22q11 deletion, higher than the rate of 0.4% estimated for adult onset cases. Because 29% of our COS patients had pre-psychotic autism spectrum disorder, we were particularly interested in the pre-psychotic developmental pattern of our COS probands with the 22q11.2 deletion. While the 22q11.2 deletion has been associated with autism, it is of interest none of our 5 22q11.2 deletion subjects had previous autism symptomatology indicating an independent pathway of development for this childhood schizophrenia subgroup. This supports recent finding in 22q11.2 deletion patients with adult onset schizophrenia patients for whom early autism spectrum symptoms also were not seen.

There may also to be an excess of 2p25.3 duplications (MYT1L) compared to the rate expected for later onset patients (86). Further, COS patients had higher rates of two additional disease-related CNVs than those reported in previous adult onset cohorts (15q13.3 deletion and16p11.2 duplication) (87).

In summary the excess of rare copy number variations in COS is striking. Their non-specificity supports a general vulnerability early in brain development that would account for the non-specificity and comorbidity seen with CNVs in Childhood Neurodevelopmental Disorders.