Prevalence of prenatal and perinatal birth complications in individuals with and without ASD-associated copy number variants

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Background

- Both genetic and environmental factors have been implicated in autism spectrum disorder (ASD) risk.
- Recent advances in identifying ASD associated genetic events, such as copy number variation (CNV), underscore the role of genetics in the etiology of ASD (Sanders et al, 2015).
- Prenatal and perinatal birth complications are also associated with increased risk for ASD (Gardener et al, 2009, 2011).
- The relationship between pre- and perinatal birth complications and genetic events associated with ASD is not well understood.
- Efforts to better understand how prenatal and perinatal complications relate to genetic predisposition in ASD highlight the importance of using a gene by environment (G x E) interaction model (Kim and Leventhal, 2015).

Objectives

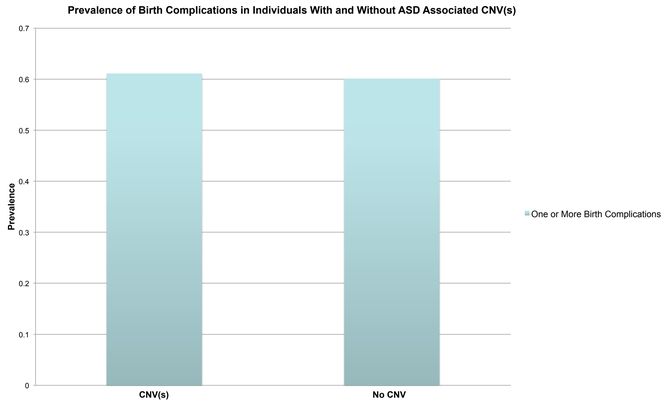
The objectives are:

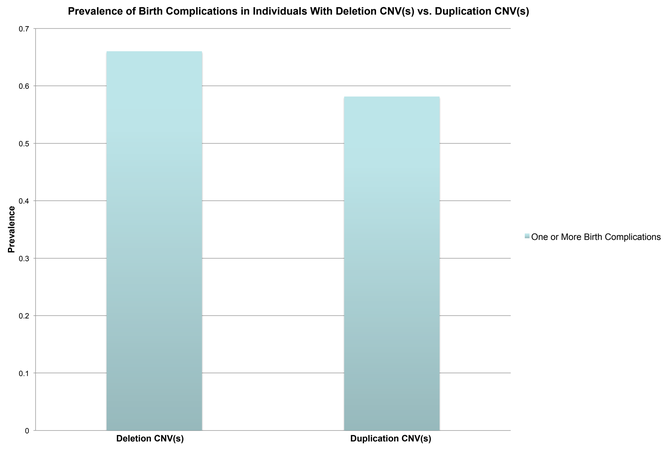
- To examine the prevalence rates of birth complications in individuals diagnosed with ASD with an ASD associated CNV and those with idiopathic ASD.
- To examine whether rates of birth complications differ between individuals with deletions versus duplication CNVs.
- To assess the prevalence of prenatal and perinatal birth complications separately within these groups.

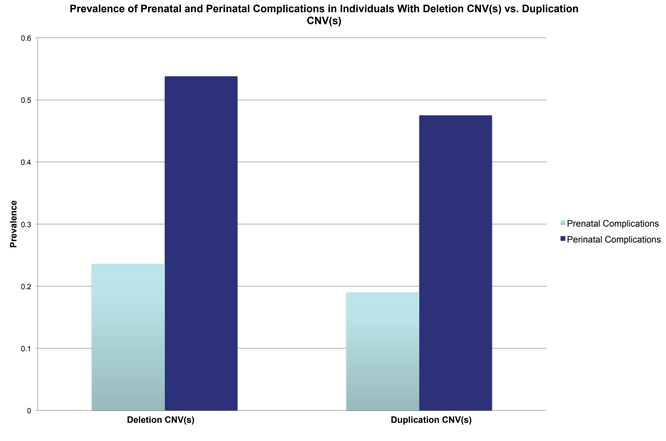
Methods

- Sample consisted of 2,765 individuals from the Simons Simplex Collection (SSC) with published sequencing results (Iossifov et al., 2014; Sanders et al., 2015).
- 397 individuals with either a likely gene-disrupting (LGD) event or both a deletion and duplication CNV were removed across all groups.
- 285 individuals with either deletion or duplications CNV(s) (and no LGD's) were identified
  - 107 individuals had a deletion CNV (Girirajan et al., 2013)
  - 178 individuals had a duplication CNV (Girirajan et al., 2013)
  - 2,083 individuals were considered "idiopathic" for analysis.
- Prenatal and perinatal data were obtained from the Pregnancy History Interview completed with parents through SSC.
  - Prenatal birth complications were defined as vaginal bleeding, low gestational age, and maternal medication usage, including psychotropic medications, beta-2 agnostics, estrogen/progesterone and tocolytics. (Froehlick-Santino et al., 2013)
  - Perinatal birth complications were defined as low birth weight (<2500 g), jaundice, respiratory distress, resuscitation, oxygen requirement after birth, presence of meconium, umbilical cord complications and low apgar scores at 5-minutes (Froehlick-Santino et al., 2013).

Results







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Results Continued

- 174 (61.1%) of cases with a CNV (either duplication or deletion) reported pre- or perinatal complications, and 1252 (60.1%) of the no-CNV group had birth complications. Non-parametric analyses examining the relationship between genetic status (CNV or no CNV) and presence of birth complications revealed no differences in rates of birth complications: X^2 (1, N = 2368) = 0.094 p= 0.759.
- 70 (66.0%) of cases with a deletion had reported pre- or perinatal complications, while 104 (58.1%) of cases with a duplication had birth complications. Non-parametric analyses examining the relationship between genetic status (deletion or duplication) and presence of birth complications revealed no differences in rates of birth complications: X^2 (1, N = 285) = 1.764 p= 0.184.
- When pre- and perinatal complications were examined separately, rates of perinatal complications were higher for both deletions and duplications (53.8% and 47.5%, respectively) than prenatal complications (23.6% and 19.0%, respectively) but no significant differences between groups were observed.

Discussion

- Children with ASD associated deletions and duplications have similar rates of birth complications compared to children without any CNVs.
- The rate of perinatal complications was higher than the rate of prenatal complications, but no significant differences between groups were found.
- These findings suggest that there is no relationship between ASD associated CNVs and birth complications; however, study exclusion criteria, which eliminated individuals with serious birth complications, restricted sample variability.
- Recent work has found an interaction between genetic events, like DRD4, and perinatal environment on temperament in preschoolers (Bersted and DeLalla, 2015), underscoring the importance of taking both factors into account.
- Examining the relationship between genetic events and pre- and perinatal environments may uncover a fuller picture of ASD susceptibility during key stages of development.
- Further work on the interactions of environmental factors and ASD associated CNVs on birth complications is needed.

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