Measuring and Predicting the Effect Size of Non-Recurrent CNVs on Cognitive and Behavioral Traits

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With the routine implementation of whole genome chromosomal microarrays and exomes in the clinic, “pathogenic” Copy Number Variants (CNVs) and single nucleotide variants (SNVs), are currently identified in 15 to 20 % of children with NDs. Reliable cognitive and neuroimaging data is available for a few clinically significant variants such as 16p11.2, 22q11.2, 7q11.23 etc… which have been extensively studied by other and our group.

However, most “pathogenic” CNVs and SNVs are “non-recurrent”. Because they are observed only once or a few times in patients, it is impossible to reach the statistical power required for individual association studies. To address this issue of undocumented CNVs and SNVs, we propose a strategy. Instead of conducting individual association studies for each mutation, we propose to model effects sizes of rare CNVs on cognitive, behavioral and neuroimaging traits relying on genetic and functional annotations. This will provide an opportunity to align a landscape of extremely rare events.

I will present results from our 16p11.2 cognitive and neuroimaging studies as well as our investigation of the genome-wide effects on cognition of rare CNVs and SNVs.