

STRONG CHILDREN'S RESEARCH CENTER

Summer 2013 Research Scholar

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ABSTRACT

Title: *The Global Developmental Inventory: A novel assessment tool applied to children with FOXG1-related disorders*"

Background:

FOXG1-related disorders are a group of neurodevelopmental disorders that feature severe developmental disability, autistic features, epilepsy, and brain morphologic abnormalities. Patients with deletions and intragenic and truncating mutations of *FOXG1* have been well described with microcephaly, hypotonia, epilepsy, severe developmental delay and corpus callosum abnormalities. Patients with duplications of *FOXG1* are less common and appear to have a different epilepsy phenotype but other aspects of their neurodevelopmental phenotype are unclear.

Objective/Methods:

We created the global developmental inventory (GDI) to explore detailed characteristics of 12 neurobehavioral areas, and applied this tool to a group of patients with *FOXG1*-related disorders. We ascertained 12 subjects with intragenic mutations of *FOXG1*, 4 subjects with deletions of 14q12 including *FOXG1*, and 2 subjects with duplications through an ongoing natural history study of *FOXG1*-related disorders. Developmental and neurobehavioral data were collected through phone interview using the GDI. Genetic information from clinical sequencing and array CGH, clinical data, epilepsy history and brain MRIs were also obtained.

Results:

The mean age of subjects at the time of the study was 6.88 years. Among the categories captured in the GDI, mean scores for impaired ambulation ($p=0.0411$) and breathing abnormalities ($p=0.0295$) were significantly higher in subjects with deletions and intragenic *FOXG1* mutations compared to those with duplications. Deletion and intragenic mutation subjects also had more intractable epilepsy as measured by greater number of anti-epileptic medications used ($p=0.00018$). We also found that subjects commonly have severe gastrointestinal motility defects, sleep disturbances, and lack of language and fine motor skills regardless of type of *FOXG1* abnormality. Review of brain MRI scans confirmed a spectrum of morphologic abnormalities of the corpus callosum in subjects with deletions and intragenic *FOXG1* mutations, while those with duplications had normal brain scans.

Conclusion:

This study allows us to make several conclusions. First, there were significant differences in regards to epilepsy severity, ambulation, and breathing abnormalities in subjects with deletions or intragenic mutations of *FOXG1* compared to duplications. Second, most individuals with *FOXG1*-related disorders exhibited a core phenotype of severe language impairment, sleep disturbance, and disordered gastrointestinal motility. Third, a spectrum of corpus callosum abnormalities was seen in deletion and intragenic mutation subjects, but not in those with duplications. The GDI is a useful tool in the measurement of neurobehavioral aspects of the phenotype in complex developmental disorders.