Williams Syndrome

Introduction

Williams syndrome (WS) is a complex genetic disorder characterized by a constellation of features including distinctive craniofacial features, developmental delay, specifically in language and cognitive abilities, unique social behavior, and a characteristic facial appearance. The syndrome is caused by a chromosomal deletion on chromosome 7q11.23 and typically affects one in 7,500 live births.

Williams Syndrome

Cognitive & behavioral profile in WS

- Unusually friendly, increased interest in social interactions
- IQ typically falls to a moderate range of mental retardation
- Major deficits in spatial processing
- Relatively strong language and face processing
- Increased use of affective prosody and social language in narratives

Neuroanatomical abnormalities in WS

- Overall brain volume decreased by about 10%, particularly attributable to reductions in parietal and occipital lobe volumes
- Regions with relatively increased gray matter volume: ventral prefrontal cortex, superior temporal gyrus, amygdala, and posterior vermis of the cerebellum
- Decreased parieto-occipital lobe volumes relative to frontal volumes, thought to lead to a more flat bending angle of the corpus callosum and cerebrum compared to typical individuals.

Two key brain networks involved in regulating social behavior

1. Ventral circuit monitoring social cognition includes:
   - amygdala, anterior cingulate, superior temporal gyrus and medial-temporal lobe nucleus
   - Social information processed in the amygdala is transferred to the orbitofrontal cortex where social responses and behaviors are selected

2. Striatum-thalamocortical loop
   - prefrontal regions: the orbitofrontal and lateral cortex and anterior cingulate
   - In charge of behavioral inhibition and includes prefrontal regions: the orbital and lateral cortex and anterior cingulate

Purpose of the present study

- Employ signal detection method (QROC) to identify brain regions most strongly associated with WS vs typically developing controls (TDCs)
- Evaluate the relationship between these brain regions, and a salient feature of the WS social phenotype: the atypically expressive and affective social language (language engagement devices, SED) in narratives.

Participants

- Controls (TDCs)
- Williams Syndrome (WS)

Methods

- VAPFC

Materials & Procedures

- MRI

Figure 1: Subdivisions of the prefrontal cortex and the orbitofrontal cortex.

Figure 2: Ventral anterior prefrontal cortex (VAPFC) volume

Discussion

- The QROC was applied to the brain regions that most significantly and specifically distinguished WS controls. Brain regions included in this analysis have been reported to be abnormal in individuals with WS.
- The VAPFC, as well as the bending angle of the corpus callosum, are strong distinguishing characteristics of individuals with WS.

Brain regions that distinguish Williams syndrome

- We utilized a signal detection method (QROC) that has rarely been used in imaging studies. QROC was instrumental in the identification of specific brain measures that are most closely associated with WS.
- Using the QROC we identified the VAPFC, and consequently elucidated its association with the use of social language in WS.
- The VAPFC, as well as the bending angle of the corpus callosum, are strong distinguishing characteristics of individuals with WS.

The relationship between brain and behavior

- The orbitofrontal cortex, which partially overlaps with the VAPFC region defined here, is a pivotal part of the ventral circuit that monitors social cognition and regulates emotional states and behavior.
- The abnormal morphology of the VAPFC may be associated with enhanced use of social language in individuals with WS.
- Thus our results associating the VAPFC with abnormal social use of language in WS provide support for the important role of prefrontal cortex abnormalities to the social phenotype in WS.

Genes to Brain to Behavior

- Our findings support that aberrant neurodevelopment of the ventral anterior region of the prefrontal cortex is an important factor contributing to the unique cerebral morphology of individuals with WS, as a consequence of haploinsufficiency of genes from the deleted region.