The Potential of Non-Invasive Brain Imaging in Understanding CAS

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Diagnostic Criteria

- Increased speech sound durations
- Increased duration of intervals between sounds and syllables
- Speech sound distortions (any substitutions are distorted)
- Abnormal sentence and lexical stress and prosodic patterns
- Speech segmentation (staccato-like speech)
Non-Differential Features

- Severe intelligibility reduction
- Inconsistency
- Increasing errors as length of utterance increases
- Groping
- Increased errors on more complex phonemes
- Speech initiation difficulties
- Awareness of errors (e.g., self-corrections)
- Automatic speech better than propositional speech
- Perseveration errors
Features Differential for other Speech Sound Disorders

- Anticipatory errors
- Transposition errors
- Weakness of the oral structures
Exclusionary Criteria

- Fast speech rate
- Normal speech rate
- Normal stress and prosody
- Smooth transitions (no segmentation)
This Talk

• Overview Methods (BRIEFLY)
• Review the very small literature
• Offer a proposal to use Genomic imaging to better understand CAS (and other speech disorders)
Non-Invasive Imaging Methods

- Structural MRI
- Functional MRI
- Positron Emission Tomography (PET)
- Image guided, robotic Transcranial Magnetic Stimulation
FOXP2 (Watkins, Vargha-Khadem et al., 2002)

• VBM with T1-weighted MRI scans in 17 family members (7 of whom had AOS)
  – AOS associated with reduced gray matter in caudate nucleus, bilaterally
  – AOS also may be associated with reduced gray matter in dorsal inferior and precentral frontal gyri
Adult Stroke-Induced AOS

- Regions of interest include Left Dorsal Prefrontal cortex, Broca’s area, insula
Genomic Imaging-A Proposal for CAS (with thanks to Dr. David Glahn)

• “Neuroimaging offers a powerful way to bridge the gaps between genes, neurobiology and behavior” (Bearden, Glahn et al, 2008)

• Neuroanatomic markers from high resolution MRI are strong candidates for neurophenotypes (endophenotypes)
What’s to Follow

• Overview of converging methodologies to examine genetic influenced on brain structure
• Examples of approach and methods in various genetic syndromes
• Including some astounding pictures of brain structures
• First, a digression into evolution (courtesy of Dr. Peter Kochonov)
Figure 2. Structural MRI data were processed using object-based-morphometry pipeline. Brain images were processed with the following steps: skull-stripping (A); RF-homogeneity correction and spatial normalization (B); hemispheric and tissue segmentation (C,D), extraction of GM and WM surfaces (E,F); Identification of sulcal surfaces using crevasse detector (G); Identification and labeling of sulcal structures (H).
Figure 3. Top part: eleven cortical sulci were used in this analysis. Bottom part: sulcal surface area, depth and length were computer for each structure.
Strategies for Investigating Neuroanatomic Endophenotypes

- Family History
  - Common genes, small effect

- Environmental Risk Factors
  - Unknown Mechanisms

- High Penetration (rare) Mutations
  - 22q11.2 microdeletion
  - Fragile X

Neuroanatomic Endophenotypes:
- Neuropil reduction
- Decreased frontal gray matter
- Cerebellar volume deficits
- Anomalous myelination
- Fronto-striatal disconnectivity

- Psychosis
- Autism
- ADHD
Correlation Maps

Controls

22q11DS
Gene-Brain-Behavior Correlation in Fragile X

A. FMRP Correlations in Females with FraX
   a. Correlation Map (r-value)

   ![Correlation Map](image)

   - negative correlation
   - correlation
   - positive correlation

   b. Significance

   ![Significance Map](image)

   - significance correlation

B. Regional Correlations with Caudate Expansion: Significance Maps
   a. FMRP

   ![FMRP Map](image)

   - signification correlation

   b. Autism Behavior Checklist Score

   ![Autism Score Map](image)

   - signification correlation

   c. Stereotypy Score

   ![Stereotypy Score Map](image)
Conclusions

• Using Non-Invasive Imaging has great potential as an endophenotype in speech disorders
• CAS likely has a genetic basis that remains unknown
• Structural Imaging is likely the way to go (e.g. DTI), functional Imaging should be useful in older children and adults with CAS