Cognitive and Behavioral Correlates of Caudate Subregion Shape Variation in Fragile X Syndrome

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The **caudate nucleus** is an important region of the brain related to cognitive and behavioral function.
Dorsolateral Caudate Head
(part of Dorsolateral Prefrontal Circuit)
Superior/Dorsal View

Circuit responsible for tasks related to general cognition
General Cognitive Functions of the Dorsolateral Prefrontal Circuit

Cognitive Flexibility
Verbal Reasoning
Solving Visual Problems
Ventromedial Caudate Body
(part of Orbitofrontal Circuit)
Inferior/Ventral View

Circuit responsible for tasks related to social, behavioral functioning
Social behavioral functions of the Orbitofrontal Circuit

- impulse inhibition
- judgment
- social tact
- irritability
- directing attention
- controlling motor activity
The Caudate Nucleus and Fragile X

- Individuals with FXS have enlarged caudate nuclei
  One of the most consistent findings in neuroimaging studies of FXS
- Size increase correlated with IQ, aberrant behavior, and FMRP levels
- Abnormal connectivity with frontostriatal circuits
Aims

• Purpose: to investigate if localized caudate enlargement is related to cognition and behavior

• Hypothesis: We expected correlation between localized size variation and cognitive/behavioral profile

  General cognitive functioning associated with dorsal caudate head size.
  Behavioral functioning associated with ventromedial caudate body size.
Participants

Ages 15-27 (Mean = 20.4, SD = 2.98)
Age and Sex Matched Groups:
  – Typically Developing Control (TD-CTL); n=37
  – IQ Control (IQ-CTL); n=26
  – Fragile X Syndrome (FXS); n=49

112 Participants Total
Cognitive and Behavioral Assessment

- **General cognitive functioning (IQ)**
  - Wechsler Abbreviate Scale of Intelligence (*WASI*)
  - Wechsler Intelligence Scale for Children III (*WISCIII*)

- **Behavioral Profile**
  - Aberrant Behavior Checklist – Community (ABC)
    - Hyperactivity
    - Inappropriate Speech
    - Irritability
    - Lethargy/Social Withdrawal
    - Stereotypy/Repetitive Behavior
Shape Values

Brain Scan:
3T Magnetic Resonance Imaging Scanner used to obtain structural scans (entire brain)

Analysis Steps:
• Caudate Delineation (Freesurfer 5.1)
• Surface Contour Mapping Analysis
Surface Contour Mapping Analysis

1. Generate medial core line through each caudate (anterior-posterior)
2. Measure distances of radial lengths from medial line to surface

3. Compare radial distances between groups

4. *Post hoc* correlation analyses between radial distances and scores from various behavioral and cognitive test values.
Local Size Differences

A. FXS vs. IQ-CTL
B. FXS vs. TD-CTL
C. IQ-CTL vs. TD-CTL

Significance shows greater radial caudate distance of subject relative to control
IQ-Size Correlation

FXS and TD-CTL: localized size increases negatively correlated with IQ
- Dorsolateral caudate head
- Ventromedial caudate body

No correlation in IQ-CTL
ABC Total Score-Size Correlation

FXS: localized size increases positively correlated with ABC Total Score
- Dorsolateral caudate head
- Ventromedial caudate body

No correlation in IQ-CTL
Discussion

Aims:
• Is cognitive functioning negatively correlated with size of dorsolateral head (FXS)?
• Is prevalence of aberrant behaviors positively correlated with size increase of ventromedial body (FXS)?

Findings:
• Lower levels of cognitive functioning is associated with increased size of dorsolateral head and ventromedial body (FXS)
• Increased aberrant behaviors is associated with increased size of ventromedial body and dorsolateral head (FXS)
Thank You

Participants and families

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Collaborators
Questions?
Supplemental Slides
ABC Subscale-Shape Correlations

FXS Group

Hyperactivity

Lethargy

Inappropriate Speech

Stereotypy

Irritability

Dorsolateral Caudate Head
(Superior View)

Ventromedial Caudate Body
(Inf/Vert View)

Dorsolateral prefrontal circuit -- Executive function

Orbitofrontal circuit -- Behavioral functioning
Dorsolateral Prefrontal Circuit

Frontal Lobe (Brodmann’s areas 9, 10) → Caudate Nucleus (Dorsolateral Head) → Mediodorsal GPi → Mediodorsal Thalamus

Caudate Nucleus (Dorsolateral Head) → Rostrolateral SNr → Lateral STN

Dorsal GPe

Mediodorsal Thalamus

Responsible for tasks related to executive function, cognitive ability
Orbitofrontal Circuit

- Frontal Lobe (Brodmann’s area 11)
- Caudate Nucleus (Ventromedial Body)
  - Dorsal GPe
  - Mediodorsal GPi
  - Rostrolateral SNr
  - Lateral STN
- Mediodorsal Thalamus

Responsible for tasks related to social, behavioral functioning