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

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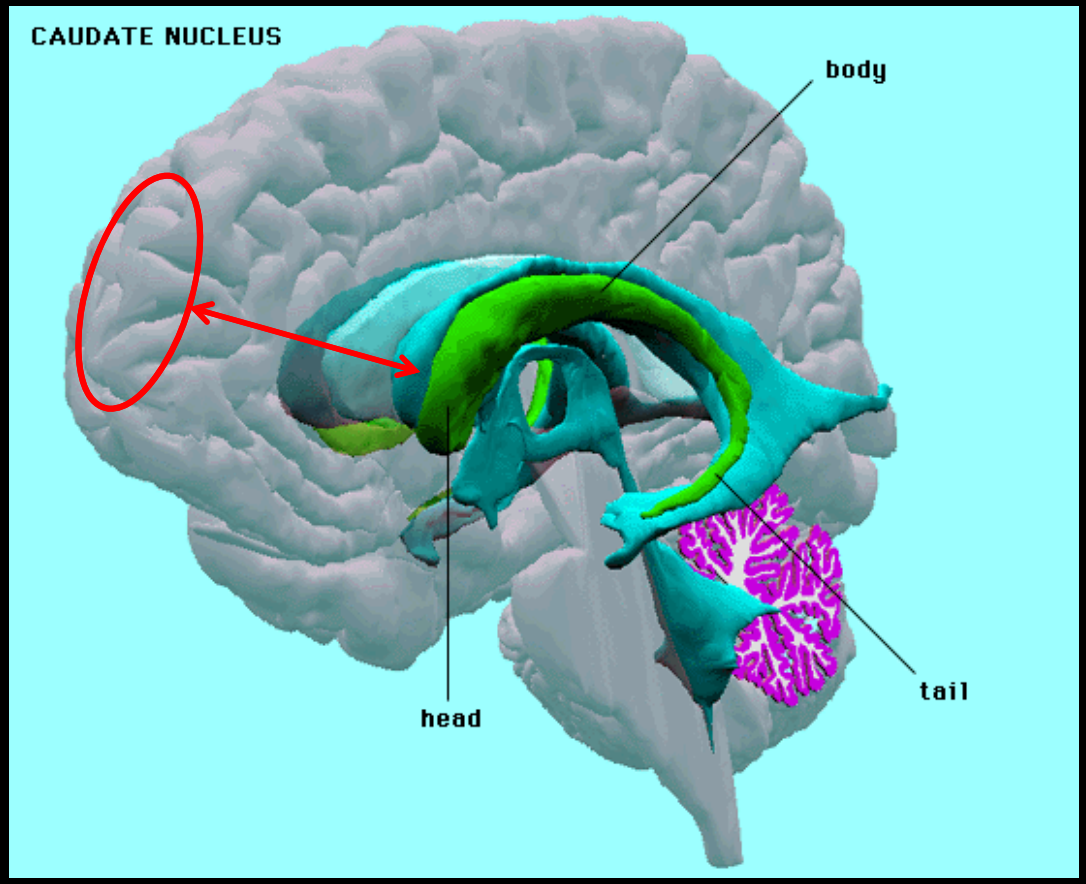
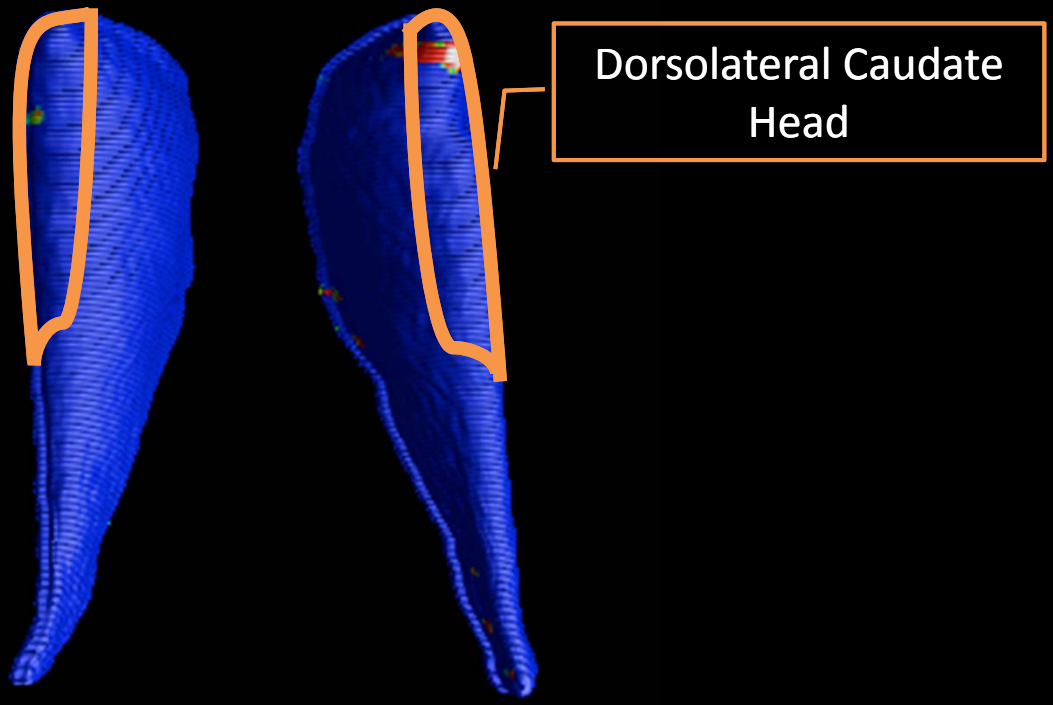
The **caudate nucleus** is an important region of the brain related to cognitive and behavioral function.



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

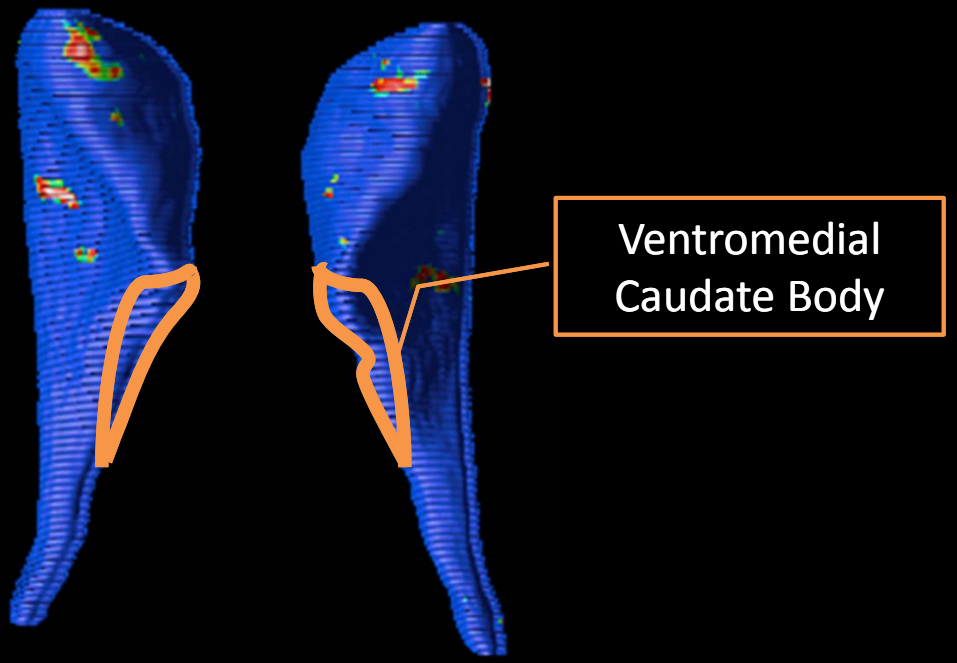
Verbal Reasoning

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.

Neuroanatomical differences → Behavioral and cognitive deficits

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:

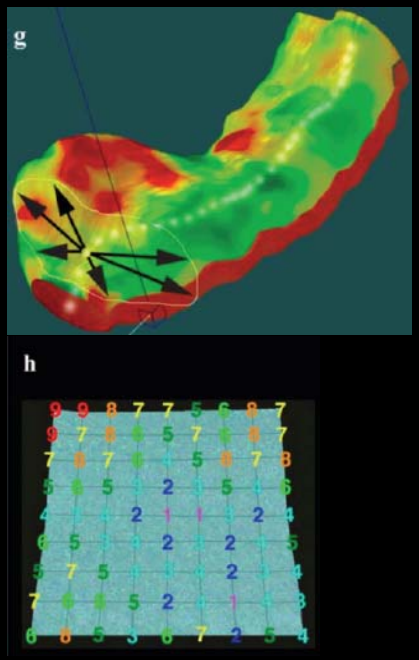
3T Magnetic Resonance Imaging Scanner used to obtain structural scans (entire brain)

Analysis Steps:

- Caudate Delineation (Freesurfer 5.1)
- Surface Contour Mapping Analysis

Surface Contour Mapping Analysis

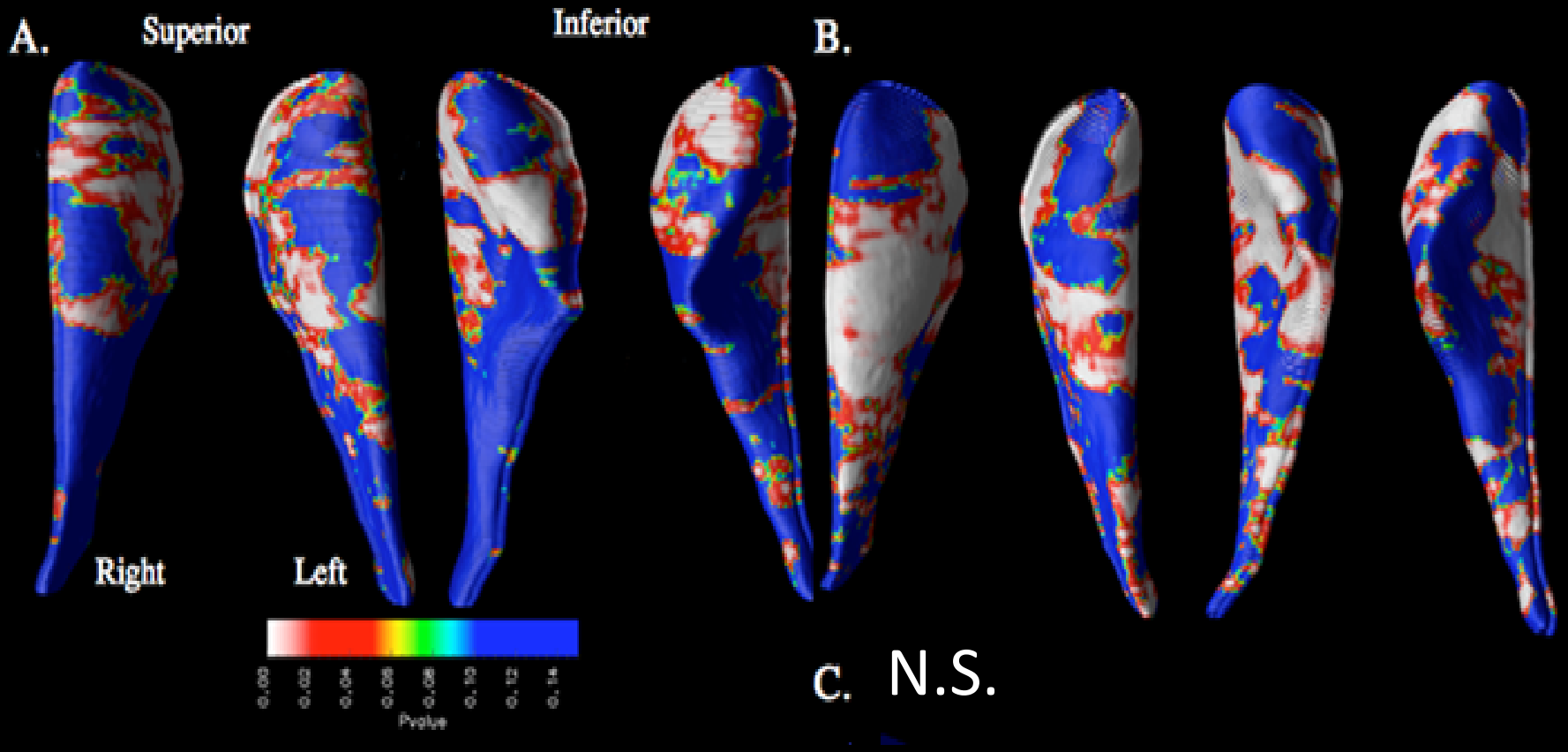
1. Generate medial core line through each caudate (anterior-posterior)
2. Measure distances of radial lengths from medial line to surface



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

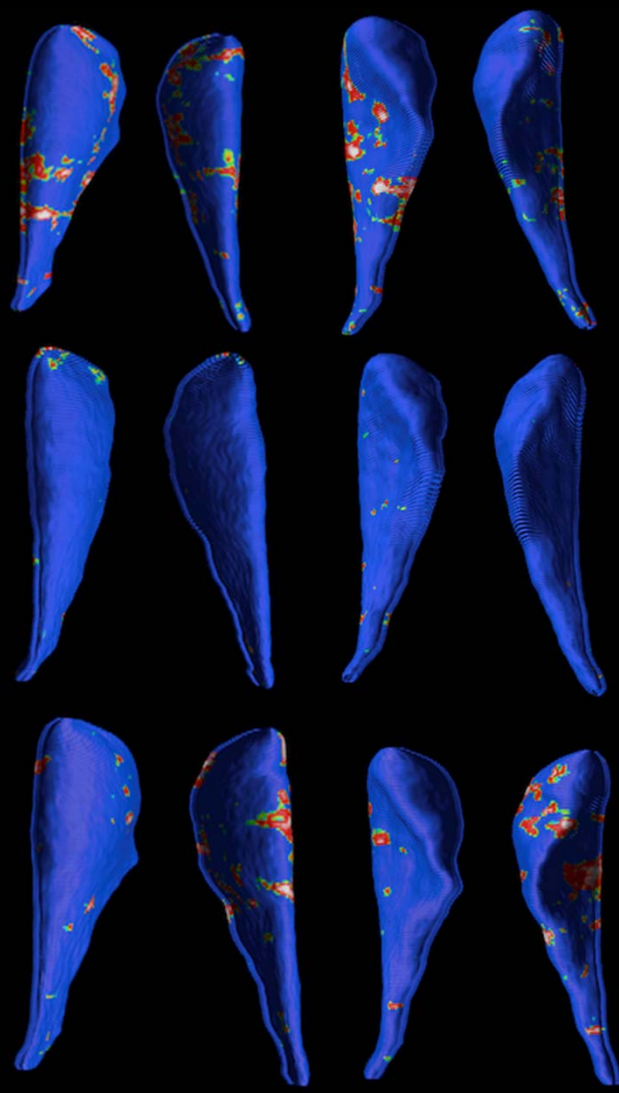


(Subject *vs.* Control)

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

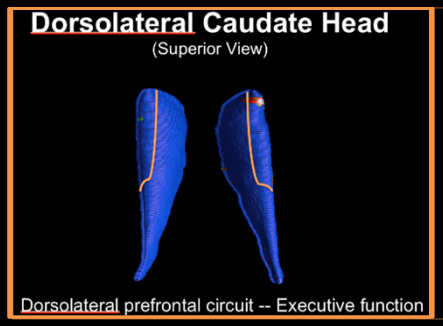
IQ-CTL

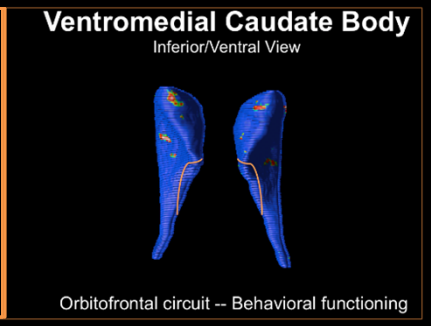
TD-CTL

FXS and TD-CTL: localized size increases negatively correlated with IQ

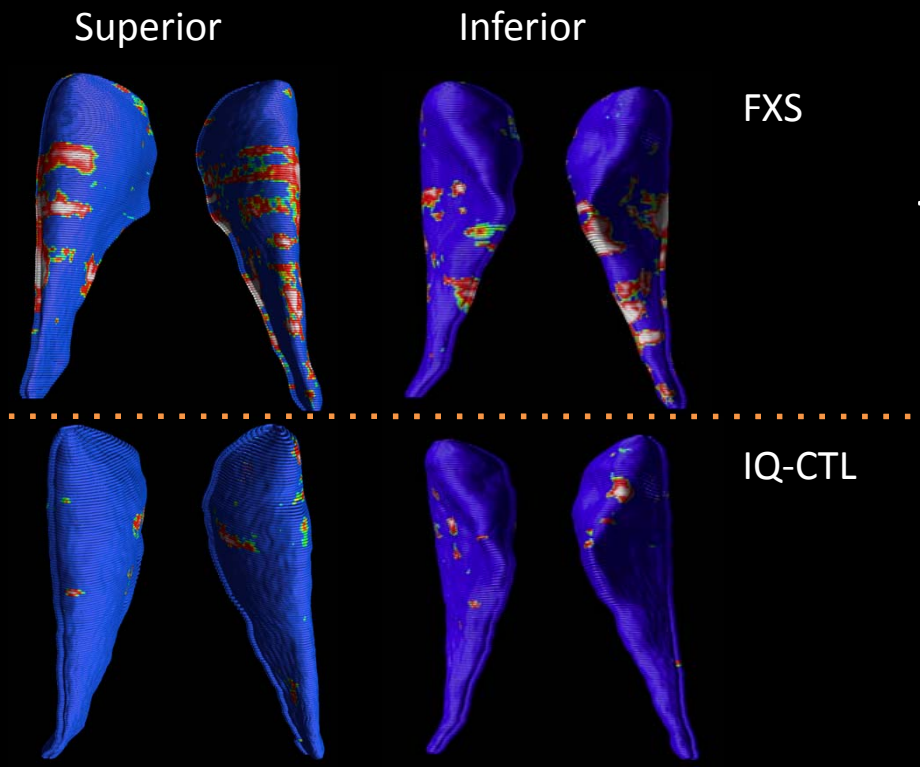
- Dorsolateral caudate head
- Ventromedial caudate body

No correlation in IQ-CTL





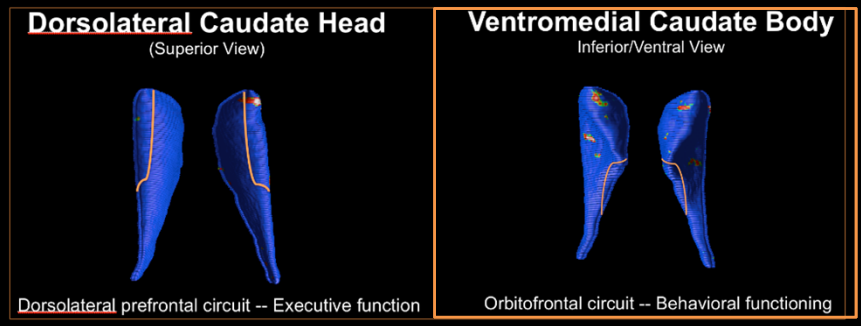
ABC Total Score-Size Correlation



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

Research Team at CIBSR

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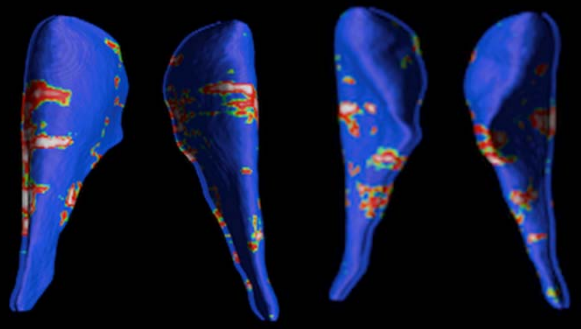
Collaborators

Questions?

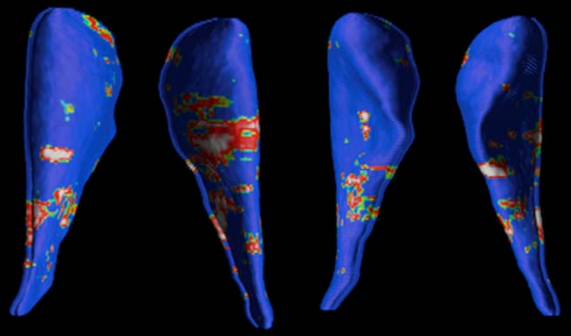
Supplemental Slides

ABC Subscale-Shape Correlations

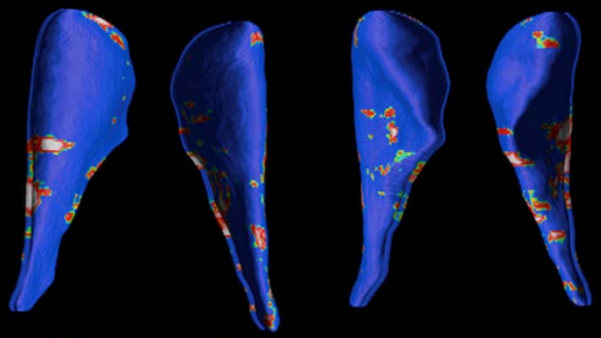
FXS Group



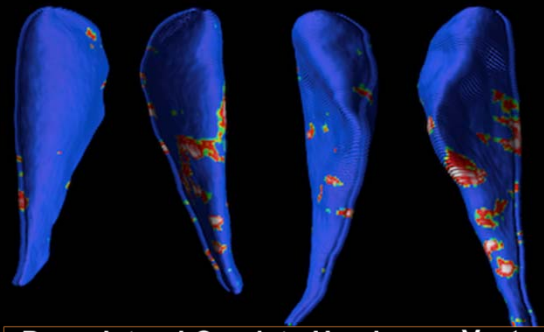
Hyperactivity



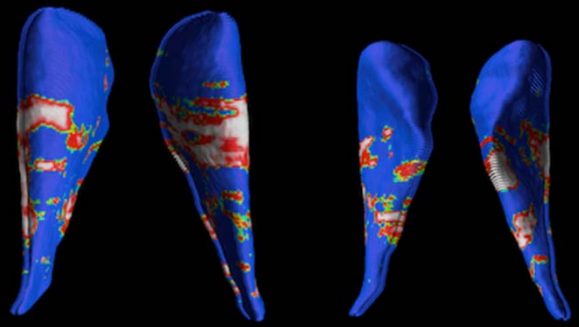
Lethargy



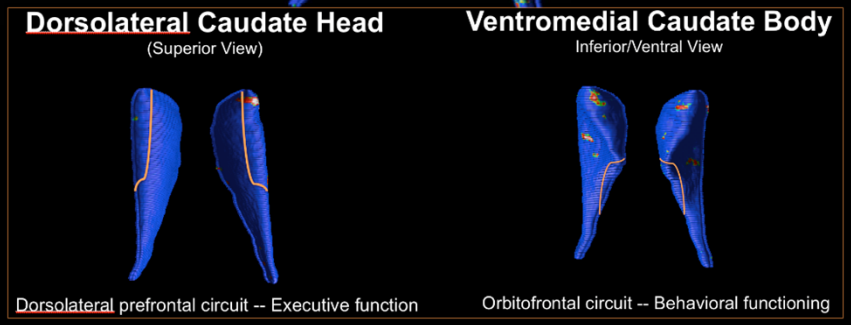
Inappropriate Speech



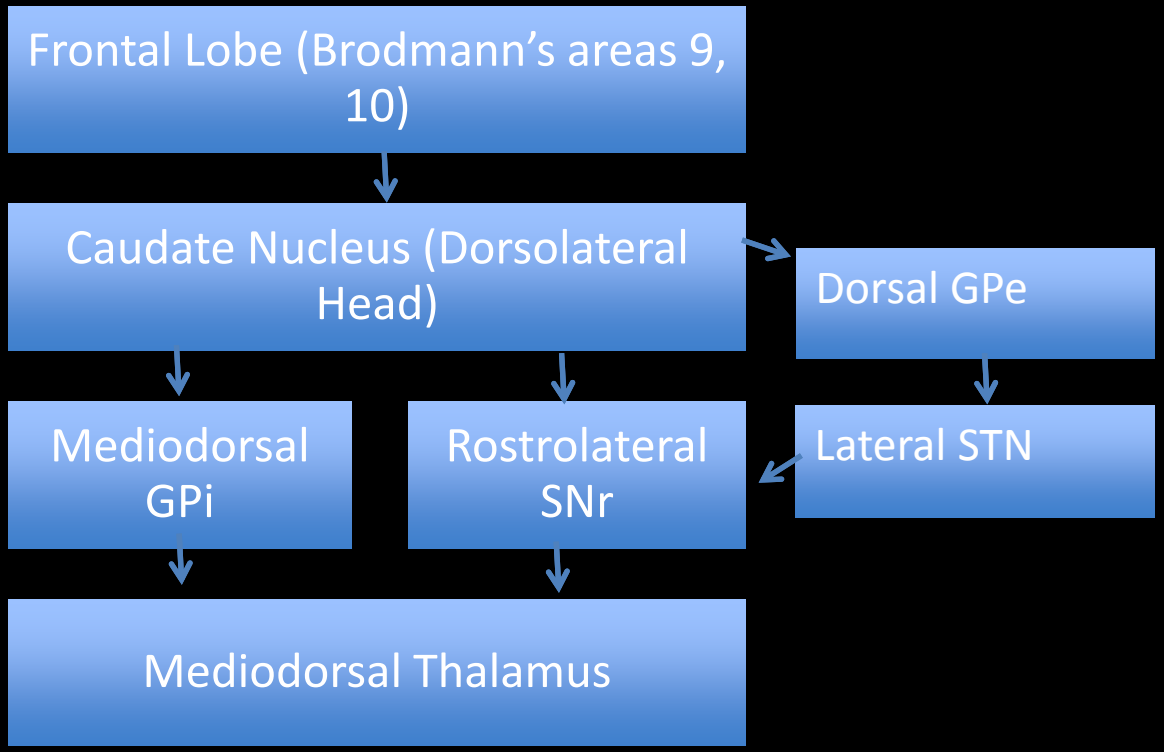
Stereotypy



Irritability

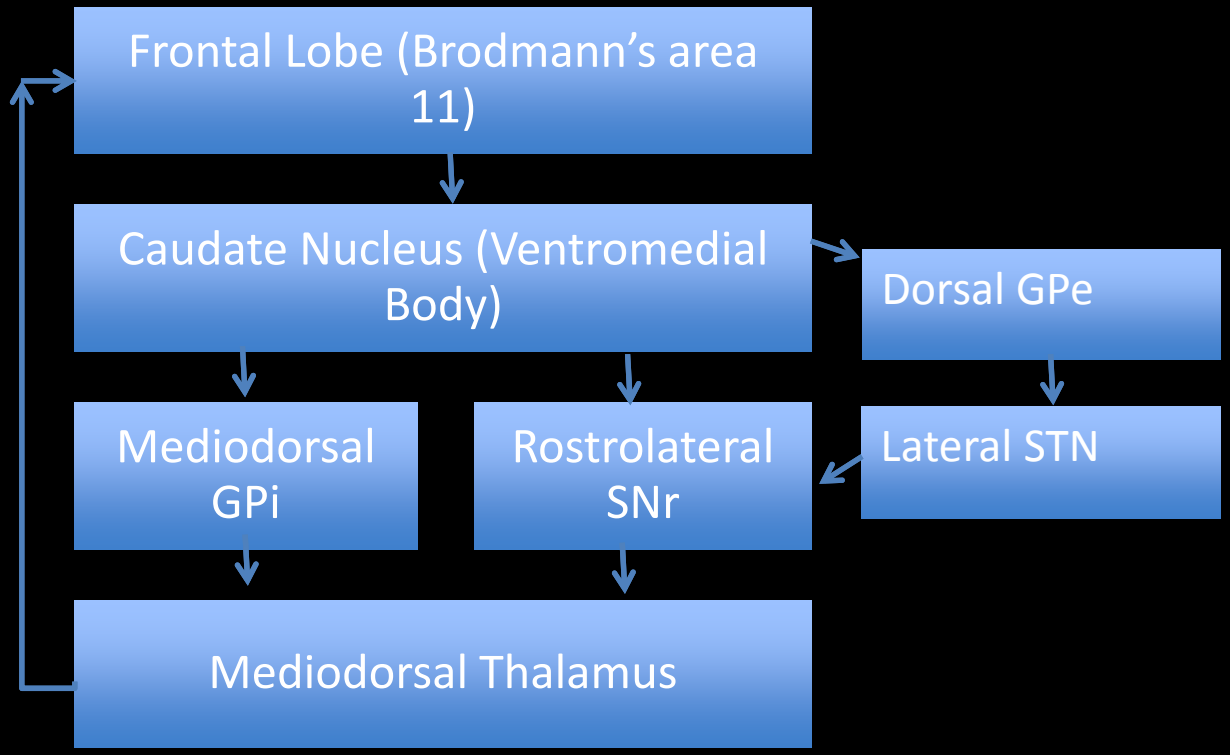


Dorsolateral Prefrontal Circuit



Responsible for tasks related to executive function, cognitive ability

Orbitofrontal Circuit



Responsible for tasks related to social, behavioral functioning