Children with Chromosome 22q11.2 Deletion Syndrome Have Smaller Putamen Than Typically Developing Children

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Chromosome 22q11.2 Deletion Syndrome

- Chromosome 22q11.2 deletion syndrome (22q11.2DS) includes DiGeorge and Velocardiofacial (VCFS) syndromes.
- Occurs in between 1:2000 and 1:4000 live births via a deletion of 3Mb pairs on the long (q) arm at the 11.2 band of one copy of chromosome 22.
- 25 to 30% of children with 22q11.2DS will develop schizophrenia in adulthood. 75% have mild prodromal psychotic symptoms.
- The putamen is part of the striatum that plays a role in motor processes and learning.
- Smaller putamen volumes are associated with poorer prognosis in patients with schizophrenia.
- Recent findings suggest the putamen may affect psychotic action as it regulates dopamine.

Overview and Purpose

- Putamen volume changes over time may serve as a biomarker of schizophrenia risk.
- This is the first measure of a longitudinal study.
- Using MRI anatomical brain scans, we investigated size differences in putamen volumes between children with 22q11.2DS and those who are typically developing (TD).

Participants

- Boys and girls ages 7 to 16 years in two groups.
- 22q11.2DS: n = 15, mean age = 12.06 years, SD = 2.85
- TD: n = 15, mean age = 11.91 years, SD = 2.51

Hypothesis

- Children with 22q11.2DS will have smaller putamen compared to typically-developing controls.

Brain Imaging Method

- T1-weighted high-resolution 3D anatomical magnetic resonance images were acquired using a 3.0T Siemens Trio scanner with Echospeed gradients and a Siemens 8-channel whole head coil.
- Imaging parameters: TR = 2.17 s, TE = 4.82 ms, flip angle = 7°, NEX = 1, 192 slices, 128 x 128 acquisition matrix, FOV = 256, sagittal acquisition with 1 mm^3 voxels, 5 min 4 sec duration.

Putamen Volume Measures

- The left and right putamen were manually outlined on each MR image slice with the tracers blind to diagnosis.
- For all steps of this process, Mango (Research Imaging Institute, U of Texas) was used for region-of-interest parcellation and volume calculations.

Figure 1— High-resolution T1-weighted MRI transverse image showing the region of interest. The putamen is outlined in red.

- T1-weighted whole brain images are imported into Mango (Research Imaging Institute, U of Texas).
- Putamen volume was calculated via manual slice by slice tracings of histology-based neuroanatomical regions of sagittal images in native space.
- Tracing Axial Criteria:
  - Crosshair Posterior Commissure.
  - Crosshair Anterior Commissure.
- Tracing Midline criteria:
  - Visible globus pallidus.
  - External capsule laterally bounds putamen.
  - Internal capsule medially and superiorly bounds putamen.
  - Anterior commissure inferiorly bounds putamen.

Results

- For total putamen volume, a significant difference was found between 22q11.2DS (M = 7956.2 mm^3, SD = 2214.77) and TD groups (M = 9984.47 mm^3, SD = 1400.61; $t(28) = 3.10$, $p < 0.01$).
- Right putamen was smaller in the 22q11.2DS group (M = 4025.2 mm^3, SD = 1107.28) versus the TD group (M = 5088.4 mm^3, SD = 753.52; $t(28) = 3.07$, $p < 0.01$).
- Left putamen was smaller in the 22q11.2DS groups (M = 3931 mm^3, SD = 1016.57) versus the TD group (M = 4896.07 mm^3, SD = 673.35; $t(28) = 3.07$, $p < 0.01$).
- Within the 22q11.2DS group, there was no difference between right and left putamen volumes ($p > 0.1$).

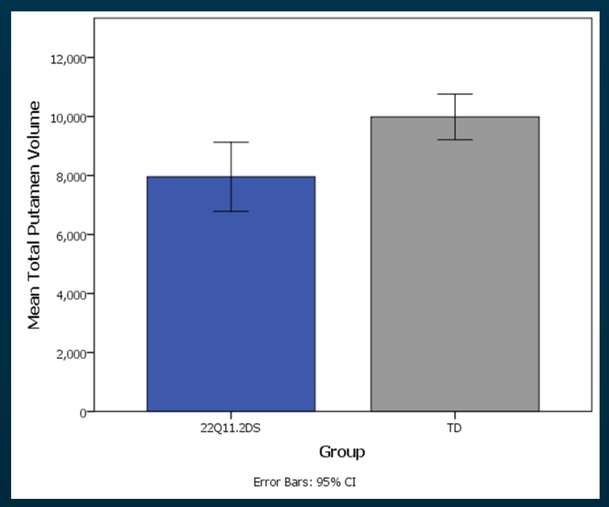

Figure 2 — Group mean (±SEM) bilateral putamen volumes.

Summary and Implications

- Children with 22q11.2DS in this study have smaller putamen than TD age-matched children.
- Smaller putamen volumes are reported in patients with schizophrenia.
- Lower volumes could be an indicator of general brain atrophy, atypical development, or both; however, given the ultra-high risk of schizophrenia, further investigation of putamen morphometry over time and in relation to prodromal symptoms is needed.

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