TARGET AUDIENCE
Neuroradiologists and neuroscientists interested in brain development.

PURPOSE
We aimed to describe the evolution of the middle cerebellar peduncle (MCP) in developing human subjects ranging from 30 gestational weeks (GW) to 18 years (Y) old, using high angular resolution diffusion imaging (HARDI) tractography.

In addition to the overall changes in the course of the MCP, number and volume of detected MCP pathways, we focused on two dissociated MCP pathways: 1) pathways from the rostral pons to the inferior cerebellum and 2) pathways from the caudal pons to the superior cerebellum. These pathways were observed in postmortem adult cerebellum in our previous study (Fig 1). We explored specifically when this dissociation becomes readily apparent.

METHODS
Imaging:
For 30 apparently healthy individuals (ages 30GW to 18Y), we performed T1-weighted MPRAGE imaging, T2-weighted turbo spin-echo imaging, and an isotropic diffusion-weighted imaging. Thirty diffusion-weighted measurements (b = 1,000 sec/mm²) and five non-diffusion-weighted measurements (b= 0 sec/mm²) were acquired on a 3T Siemens MR system with TR= 10 sec; TE= 88 msec; δ = 12.0 ms; Δ = 24.2 ms; field of view= 22 cm; slice thickness= 2.0 mm; matrix size= 128x128, iPAT= 2.

Diffusion Data Reconstruction for Tractography:
Diffusion Toolkit and TrackVis (http://trackvis.org) were used to reconstruct and visualize tractography pathways. A HARDI reconstruction algorithm was selected with a streamline approach and an angle threshold of 45°. The color-coding of tractography pathways was based on a standard RGB code applied to the vector between the end-points of each fiber.

Tract Delineation and Quantification:
A coordinate-based tractography atlas (Catani & Thiebaut de Schotten, 2008) was used to guide ROI placement in order to delineate the middle cerebellar peduncle.
Fractional anisotropy (FA), number of streamlines, and length of tracts were quantified in each subject. Number of streamlines was corrected using the information of the length of pathways.

RESULTS
Sample MCP tracks are provided in Fig 2 with a single slice b0 image provided for gross anatomical reference (actual ROI placement utilized multiple slices).
1. The number of MCP streamlines identified or detected increased progressively with age until initially plateau at about 3Y.
2. Streamlines between the rostral pons and inferior cerebellum hemisphere were detected at an earlier age than those between the caudal pons and superior cerebellum.
3. Starting at 6Y, the total MCP bundle became significantly thicker, and, at about that age, the caudal pons to superior cerebellum pathways became prominent.
4. At 40GW, the MCP consists almost entirely of pathways apparently terminating deep within the cerebellum, with only few pathways branching to the cerebellar cortex. Pathways to the cerebellar cortex start to appear at 3Y, and their numbers increased with age.
5. In quantitative analyses, mean FA and average streamline length increased with age in the first 3 years post-term (40GW to 3Y) (Two-tailed t-test, p < 0.001).

DISCUSSION and CONCLUSION
This work appears to demonstrate a bi-phasic development for the MCP pathways. The first phase, occurring from term to 3Y, would be dedicated mainly to the development of the rostral pons to inferior cerebellum pathway. While the second phase, completing about 6Y, would correspond to the development of the caudal pons to superior cerebellum pathway. It is likely that the major cause of these changes in diffusion properties is related to the degree of myelination of existing tracks.