Radial and Tangential Migrational Pathways Revealed by Diffusion Tractography

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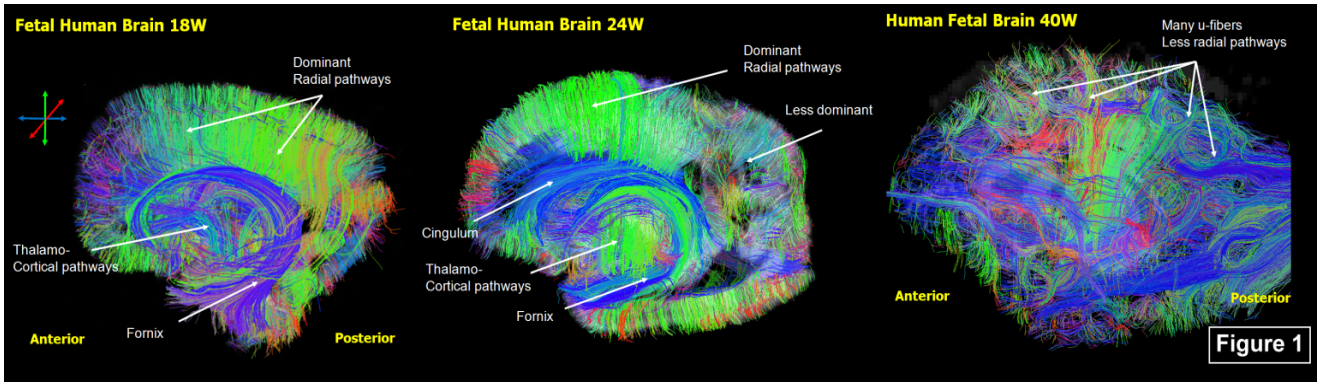
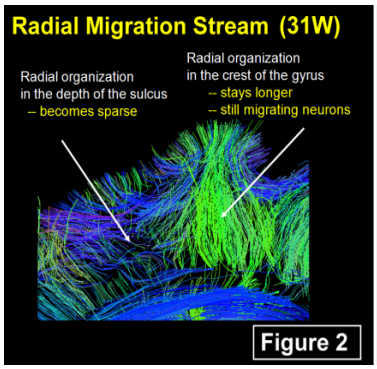
Introduction: In the human brain, there are two major migration pathways: Radial neuronal migration occurs from the 8th gestational weeks (W8) **[1]** and completes between W24 and W40, depending on brain regions **[2]**, while the other migration pathways originate from the ganglionic eminence constitutes an eminence of tightly packed migrating cells above the thalami and the caudate nucleus, and disappears by the age of 1 year **[2]**. High-angular resolution diffusion imaging (HARDI) has been proposed as an alternative to diffusion tensor imaging (DTI) for improved resolution of crossing fiber pathways **[3]**, and is effective for delineating the structural changes that occur in developing fetal (preterm) brains **[4, 5]**. Here, we applied HARDI tractography to intact whole postmortem fetal human brains to explore the 3-dimensional regression of the radial and tangential migration pathways.

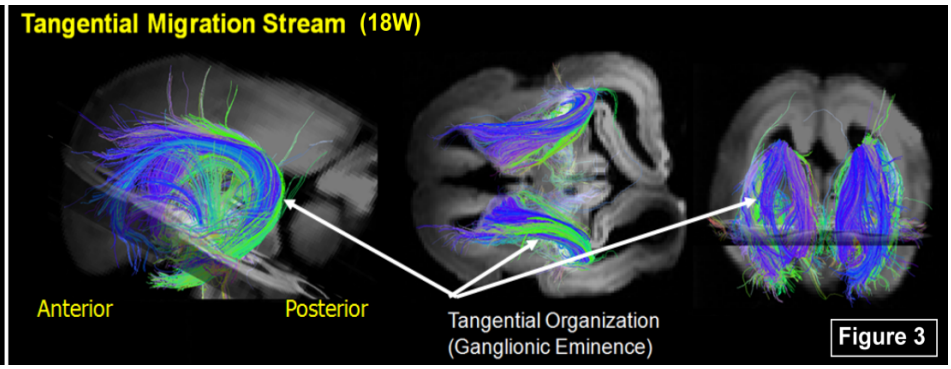
Method: We imaged human fetal brain specimens of post-gestational week (W)18, W20, W22, W24, W31, W38, and W40 (two samples for each time point), using a 4.7T Bruker Biospec system. We performed a 3D diffusion-weighted spin-echo echo-planar imaging (EPI) sequence (61 measurements), TR/TE 1000/40 ms, with b = 8,000, small/large delta = 12.0/24.2 ms, spatial resolution of 415 x 500 x 550 μm for W18-24, 525 x 525 x 600 μm for W31, and 700 x 830 x 860 μm for W38 and 40. The color-coding of fibers is based on a standard RGB code (Green: dorsal-ventral, Red: right-left, Blue: anterior-posterior).

Results: ***Radial migration pathways:*** The dominant radial organization at W18 from the ventricular margin to the pial surface is likely to represent radial migration along radial glial fibers, and gradually diminishes first in dorsal parieto-occipital regions and later in ventral frontal and temporal regions, and gives rise to a variable degree of horizontal organization that is more pronounced first in dorsal parieto-occipital regions and later in ventral frontal and temporal regions (**Fig. 1**). Such maturation of radial pathways occurred prior to or simultaneous with gyral formation in each brain area. This radial organization also showed regional variation: radial organization persisted longer in the crests of the gyri than at the depths of the sulci (**Fig. 2**). ***Tangential migration pathways in the ganglionic eminence:*** Tangential pathways associated with the lateral ganglionic eminence (**Fig. 3**) gradually disappear from 18 through 40W (**Fig. 1**), which is consistent with the disappearance of the migrational streams and elongated glial processes in the human brain as they move tangentially in the ganglion eminence before migrating to the cortex or thalamus (e.g. **[6]**). ***Caveat:*** Not all structures that disappear are migrational streams or radial glia. Disappearance of some tracts likely represent natural pruning of axons known to take place due to lack of appropriate targeting.

Conclusion: Our results show the usefulness of HARDI tractography to image both radial and tangential migrational streams in fetal human brains, and suggest that regional regression of radial organization and regional emergence of fetal brain axonal connectivity proceed in general from postero-dorsal to antero-ventral with local variations related to the later appearance of gyri and sulci.







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