

## Development of visual cortex in infants

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Target Audience: Researchers from a broad range of backgrounds interested in the application of fMRI methods in developmental of visual neurosciences.

Purpose: The most widely used technique to study the development of the visual system in infancy has been the VEP, showing that visual temporal resolution develops very rapidly after 7 weeks of age<sup>1</sup>. From 15-20 weeks, VEPs responses reflects discrimination between coherent and incoherent motion, showing directional motion selectivity<sup>2</sup>. Orientation-driven VEPs are measurable at 5-7 weeks, while motion-direction VEPs emerge later and develops separately<sup>3</sup>. But there is very limited information about the development of the various visual cortical regions. It is commonly assumed that lower cortical visual areas (V1-V2, including the retina and LGN) develop first, followed by higher regions (V3-V6-MT). In adults, motion direction selectivity is mediated by an extensive network of areas (V1, V3, V6, LO, MT, VIPs, Pre-Cuneus, PIVC)<sup>4,5,6</sup>. Here we investigate with fMRI if this neural network is functional also in infancy.

Methods: Eleven (4 females) healthy, full-term, awake infants, mean age 7 weeks, were scanned by a 1.5T MR scanner (GE Healthcare, USA). Data from 2 of them were not included in the analysis because of movement artifacts. The MR protocol comprised the acquisition of a 3D T1w FSPGR sequence (TR/TE=12.28/5.14, isotropic voxel =1x1x1mm<sup>3</sup>), and a fMRI session of three different series (GRE-EPI, TR/TE=3000/50, FA=90°, FOV=240mmx240mm, matrix=96x96, slice thickness=3mm). fMRI experiment included two series of 84 time points (4'12" duration, block design, 6 cycles of alternating "A" and "B" condition, each lasting 21s) each with a specific stimulus (1.High contrast flow motion versus blank; 2.High contrast flow motion versus random noise<sup>4</sup>). In five subjects a resting state fMRI series (120 time points, 6' duration, no stimulus presentation) was successfully acquired during the spontaneous sleep of the newborn. Stimuli were generated in Matlab and displayed on LCD goggles (Resonance Technology). Fixation of infants gaze was monitored by an infrared camera installed on the goggles (sample frequency 60 Hz). The same MR protocol was repeated in five healthy adults (4 females, mean age=35years). The study was approved by IRB and written informed consent was obtained by all subjects or parents. Data analysis was performed by using BrainVoyager (Brain Innovation). Data preprocessing included mean intensity adjustment to compensate for interscan intensity differences, temporal interpolation and re-sampled to compensate for slice dependent time differences (sinc function), 3D motion correction (sinc interpolation) and high-pass temporal filtering. Finally, newborn data were transformed into the AC-PC coordinate system, whilst adult data were transformed into the standard Talairach's space. For each subject, BOLD responses were analyzed using a GLM modeling the regressor of interest (by convolving a box-car function for each stimulation block with a gamma variate function for the hemodynamic response) and six spurious movement-regressors (outputs of the 3D motion correction procedure). The first stimulus (motion versus blank) was used to select a region with very strong response (focus) in the calcarine cortex, used as seed. A correlation map was generated by using the signal registered in this seed (p<0.05). Afterwards this map was used as mask of motion perception cortical regions in the GLM analysis of the second stimulus (motion versus noise) which identified those areas selective to motion coherence. Resting state series was used to study the correlation between the areas found in analyses described above.

Results: Our data confirm, using fMRI and eye tacking recording, that neural mechanisms selective for motion direction are already well developed and established at 7 weeks of age. This mechanism involves a network of visual areas responsive to flow versus random motion and the visual-vestibular associative cortex that mediates the ego-motion perception. The network is very similar to that of adults<sup>7,8</sup>, including primary visual cortex V1, MT+, the posterior occipital cortex V6, as well as the cuneus and the Posterior Insula associative Vestibular cortex PIVC (FIG.1A). The percentage of BOLD signal shows that V1, as in adults, has a small preference for random noise compared to coherent motion, as opposed to MT+. The signal to noise response to flow is stronger than for random motion both in infants and in adults, and the modulation of the BOLD response is similar in MT and V6. Correlation analysis (FIG. 1B) suggests an absence of correlation between V1 and MT in infants that increase during development but a stronger functional connectivity between the cuneus MT and V6 that decreases over time as well as between PIVC L and R and between PIVC and the ipsilateral V6.

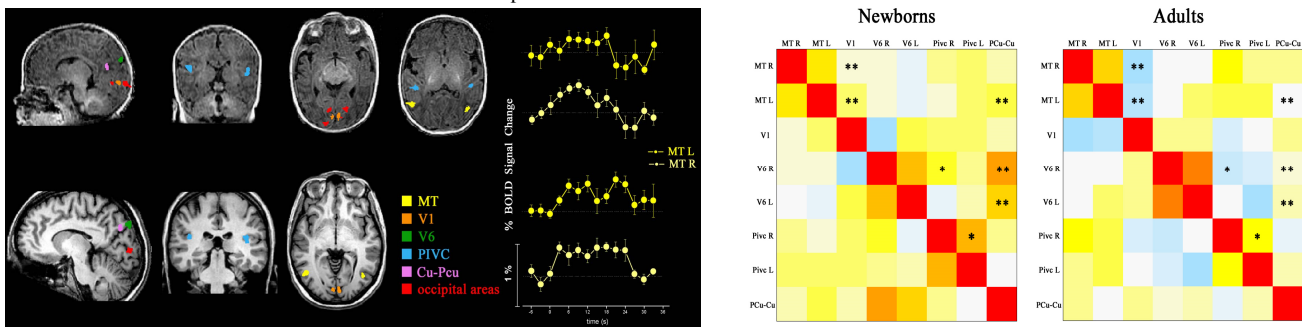


Figure1. A. Areas selective to coherent motion in a newborn (top) and adult (bottom) and respective BOLD response in Left and Right MT. B. Mean correlation matrix for newborns and adults.

Discussion and Conclusion: Medio-temporal cortex is selective to flow motion at 1.5 months of age and the observed pattern of responses indicates that the motion area network is well established very early. This surprisingly faster development of associative visual cortex contrasts with the relative immature connectivity between V1 and MT suggesting a possible alternative V1-independent input to MT. At the same age the cortical mechanisms responsible for perception of ego motion are fully functional. Both the maturity of visual-vestibular connections shown by our data and the concurrent development of the two neural mechanisms suggest that we need to perceive self motion in order to perceive motion in the outside world, and vice versa.

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