

Microglial dynamics in the developing and early postnatal human brain

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The regional heterogeneity of microglia is well-documented in the adult human and rodent brains. Microglia proliferate in the adult at a rate of 0.08–2% in humans and 0.5–0.7% in rodents. They appear by the 4th gestational week (gw) in the telencephalon and are thought to colonise the brain by 24 gw. Their precise spatiotemporal dynamics during development and in postnatal life remain unclear. With ethical approval from the above centres, frontal and temporal areas in 92 human control cases are currently being studied (age range 5 gw to 18 years). Clustering of microglial signature genes in RNA-seq data from 322 tissues was tested by region of interest and timepoint (5–22 gw). Preliminary results from the 25 gw to 2 years age range show very little microglial proliferation during the third trimester. Microglial morphology becomes more consistent with the mature adult form in the grey and white matters after 35 gw. Microglial proliferation increases dramatically soon after birth and by about 5 postnatal weeks, proliferation decreases sharply. RNA-seq data demonstrate clustering of microglial signature genes from the 5th gw in the cerebral cortex, the choroid plexus, the cerebellum and the spinal cord. These findings suggest that microglial proliferation is a postnatal event and that microglial signature genes cluster early by anatomical regions known to have differential microglial profiles in the adult. This work is part of a larger study investigating microglial dynamics across the lifespan in humans from the 4th gestational week until old age.