Studies on the development of the human cortex suggest that the insula is the first cortical structure to develop in the fetus. The process of cortical development begins in the 6th week of fetal life in an inferior cortical region. This region will later fold to become the limen insula.

Afif et al. carried out a macroscopical study on 21 human fetal brains, showing no anomalies, from 13 to 28 Gestational age(GWs). Particular focus was given to morphological appearance during the development of insular and periinsular structures, especially the gyration and sulcation of the insula, central cerebral region and opercula, as well as the vascularization of these regions. The periinsular sulci and the central (insular and cerebral) sulci were the first macroscopical structures identified on the lateral surface of the human fetal cerebral hemisphere with earlier development on the right hemisphere.

They described five stages of insular gyral and sulcal development closely related to gestational age:

stage 1: appearance of the first sulcus at 13-17 GWs, stage 2: development of the periinsular sulci at 18-19 GWs, stage 3: central sulci and opercularization of the insula at 20-22 GWs, stage 4: covering of the posterior insula at 24-26 GWs, stage 5: closure of the sylvian fissure at 27-28 GWs. They provided evidence that cortical maturation (sulcation and gyration) and vascularization of the lateral surface of the brain starts with the insular region, suggesting that this region is a central area of cortical development <sup>1)</sup>.

## 1)

Afif A, Bouvier R, Buenerd A, Trouillas J, Mertens P. Development of the human fetal insular cortex: study of the gyration from 13 to 28 gestational weeks. Brain Struct Funct. 2007 Dec;212(3-4):335-46. doi: 10.1007/s00429-007-0161-1. Epub 2007 Oct 26. PMID: 17962979.

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