

## **Semilobar Holoprosencephaly with Midline “Seam:” A Morphogenetic Model Based upon Mri Analysis**

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A uniform topology of core forebrain structures characterized 7 of 16 of an MRI-based series of brains with HPE, imaged at the Kennedy Krieger Center and analyzed at the MGH CMA. Structures which are normally paired and separated on right and left sides of forebrain are instead conjoined in a midline gray matter continuum or “seam.” These are suprachiasmatic diencephalon, caudate and accumbens heads, and neocortex. Throughout its rostral to caudal extent, the seam abuts the superior midline of the ventricular system. In rostral relation to this continuum, there is no hemispheric fissure. Caudally there is a hemispheric fissure within which gyrated neocortical surfaces oppose each throughout its depth. However, in the depths of the fissure, left and right neocortex are conjoined by gray matter. Caudally the seam terminates at the callosum. Abruptly in the depths of the fissure, in dorsal relation to the callosum, the left and right neocortex is normally separate. Lamina terminals, septal structures including septum pellucidum, and fornix are absent. The supradiencephalic limb of the choroidal fissure is widely splayed but without choroid plexus. All 7 brains represent the semilobar form of the malformation with conjoined claustra. Otherwise the topologies of forebrain structures, brain stem and cerebellum appear normal. Whereas this topology appears from our analysis and our survey of photographs published in the literature to be a prevalent one, it has not to our knowledge been previously recognized and characterized. It distinguishes within the midline of the telencephalic anlage a developmental, presumably early inductive, failure of specification of midline structures. It dissociates in this zone from the specification failure a paramedian failure of differential growth necessary to vesicle evagination along the midline telencephalic anlage. This contrasts with what appears to have been normal specification and patterns of differential growth along the diencephalic – telencephalic line of evagination.

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