Pediatric Neurology 63 (2016) 23–38

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Topical Review

Telencephalic Flexure and Malformations of the Lateral Cerebral (Sylvian) Fissure

Harvey B. Sarnat MS, MD, FRCPC [a,b,c,d,*], **Laura Flores-Sarnat MD** [a,c,d]

[a] *Department of Paediatrics, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada*
[b] *Department of Pathology and Laboratory Medicine (Neuropathology), Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada*
[c] *Department of Clinical Neurosciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada*
[d] *Alberta Children's Hospital Research Institute, University of Calgary, Calgary, Alberta, Canada*

ABSTRACT

After sagittal division of the prosencephalon at 4.5 weeks of gestation, the early fetal cerebral hemisphere bends or rotates posteroventrally from seven weeks of gestation. The posterior pole of the telencephalon thus becomes not the occipital but the temporal lobe as the telencephalic flexure forms the operculum and finally the lateral cerebral or Sylvian fissure. The ventral part is infolded to become the insula. The frontal and temporal lips of the Sylvian fissure, as well as the insula, all derive from the ventral margin of the primitive telencephalon, hence may be influenced by genetic mutations with a ventrodorsal gradient of expression. The telencephalic flexure also contributes to a shift of the hippocampus from a dorsal to a ventral position, the early rostral pole of the hippocampus becoming caudal and dorsal becoming ventral. The occipital horn is the most recent recess of the lateral ventricle, hence most vulnerable to anatomic variations that affect the calcarine fissure. Many major malformations include lack of telencephalic flexure (holoprosencephaly, extreme micrencephaly) or dysplastic Sylvian fissure (lissencephalies, hemimegalencephaly, schizencephaly). Although fissures and sulci are genetically programmed, mechanical forces of growth and volume expansion are proposed to be mainly extrinsic (including ventricles) for fissures and intrinsic for sulci. In fetal hydrocephalus, the telencephalic flexure is less affected because ventricular dilatation occurs later in gestation. Flexures can be detected prenatally by ultrasound and fetal magnetic resonance imaging and should be described neuropathologically in cerebral malformations.

Keywords: hemimegalencephaly, holoprosencephaly, lissencephaly, operculum, schizencephaly, Sylvian fissure, telencephalic flexure

Pediatr Neurol 2016; 63: 23-38

Introduction

In the human embryo at 4.5 postconceptional weeks of gestation, the mantle of the prosencephalic vesicle thins in the sagittal midline as growth of a sheet of primitive meninx forms the falx cerebri, sagittal sinuses, and associated leptomeninges that deepen the interhemispheric fissure. Simultaneous prosencephalic growth in a mediolateral gradient of the horizontal axis causes "outpouching" of the forebrain to form two primitive oval-shaped telencephalic hemispheres. This division of the prosencephalon is sometimes termed *cleavage*. The primitive prosencephalic cerebral mantle exhibits thinning in the midline at the time of lateral outpouching. Although the term *cerebral mantle* usually is applied to more mature brains, it may be defined as the neural parenchyma between the ventricular and the pial surface of the cerebral vesicle regardless of the type or maturity of neuroepithelial cells or their arrangement, hence

Presented in preliminary form at the annual meeting of the Canadian Association of Neuropathologists, Ingonish, Nova Scotia, Canada, October 15 to 17, 2009, and as invited speakers at the annual meeting of the Mexican Association of Neuroradiology, Puerto Vallarta, Mexico, September 17 to 19, 2009.
Article History:
Received July 12, 2015; Accepted in final form May 4, 2016
* Communications should be addressed to: Dr. Sarnat; Alberta Children's Hospital; 2888 Shaganappi Trail NW; Calgary, Alberta T3B 6A8, Canada.
E-mail address: harvey.sarnat@albertahealthservices.ca

0887-8994/$ – see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pediatrneurol.2016.05.005

also exists in the prosencephalon. Beginning at seven to eight weeks of gestation, the posterior third of the fetal telencephalon bends or rotates posteroventrally, diagrammatically illustrated by O'Rahilly and Müller[1] and depicted here in another simplified line drawing (Fig 1). This folding of the hemisphere thus forms the operculum and future lateral cerebral or Sylvian fissure, a term applied from about 38 weeks of gestation, after the frontal and temporal lips of the operculum come together so that the insula, sometimes regarded as a third lip, deepens to no longer be exposed. The present description of the telencephalic flexure is a neuroembryologic review of the origin and ontogenesis of the lateral cerebral or Sylvian fissure as it relates to the major lobes of the brain and the lateral ventricles during normal development and in certain major cerebral malformations. Some aspects remain speculative because of a paucity of data. It is surprising that the formation of the Sylvian fissure has been so little addressed in the neuroembryology literature, despite its profound impact on mature cerebral structure and function.

Development of the lobes of the cerebrum

The initial "primitive" telencephalon at five to six weeks of gestation (postconceptional age, based on obstetrical history, fetal morphometrics, and histologic maturation of the brain and other organs) does not yet have a cortex because the first wave of radial migration from the subventricular zone to the cortical plate is only about to begin. Except for a preplate plexus of neurons and processes that will become the molecular and subplate zones of the fetal cortical plate, the primitive telencephalon is undifferentiated and cannot yet be designated as lobes of the forebrain. Thalamocortical axons have not yet projected, in part because they do not yet have target neurons to approach. Figure 2 is a montage showing photographs of the normal developing telencephalic hemisphere, including the lateral ventricles, in human fetuses at four gestational ages.

The telencephalic flexure is important for anatomic relations of the mature cerebral cortex relative to the primitive telencephalic hemisphere. These positional changes are described by O'Rahilly and Müller,[1] Bayer and Altman,[3] and other human neuroembryologists. They may be summarized as follows: (1) the posterior pole of the primitive telencephalon becomes not the occipital lobe, but the temporal lobe; (2) both the dorsal (frontal) and ventral (temporal) lips of the Sylvian fissure are derived from the ventral margin of the primitive telencephalon, of importance for genetic gradients in normal development and in

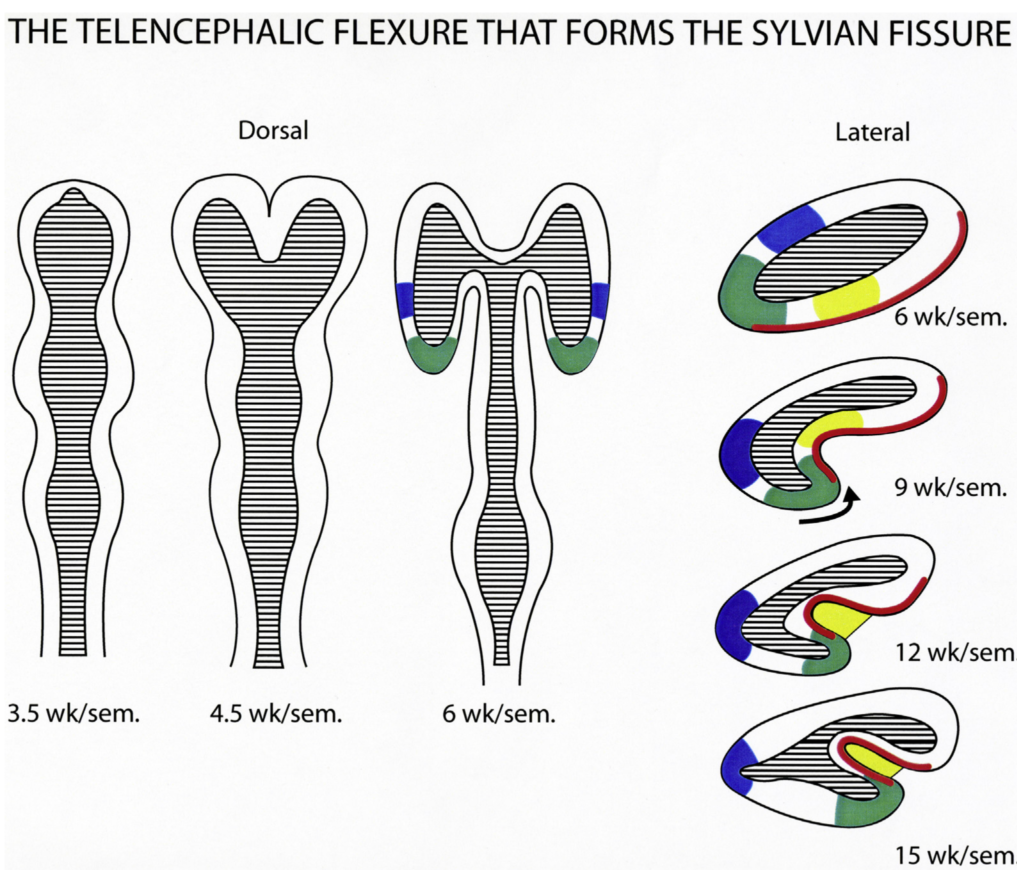

FIGURE 1.
This drawing of the telencephalic flexure illustrates its development from a ventral bending of the telencephalic hemisphere to form the operculum and finally the Sylvian fissure. The posterior pole of the primitive telencephalon before 9 weeks becomes the temporal (green), not the occipital, lobe. The occipital lobe derives from the dorsal wall of the primitive telencephalon (blue); the insula derives from the ventral wall (yellow). Both lips of the Sylvian fissure are from the ventral margin of the primitive telencephalon, so that defective ventralizing genes in the vertical axis would be expressed in the cortex forming both the frontal and temporal lips. wk/sem. = gestational weeks/*semaines* (French) or *semanas* (Spanish). (Illustration by Laura Rodríguez-Flores, graphic designer) Reproduced with permission from Sarnat et al.[2]