Chapter 21
Reelin and Lissencephaly

Elena Parrini and Renzo Guerrini

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1 Introduction

The development of the human cerebral cortex is a dynamic process that can be divided into partially overlapping stages occurring during several gestational weeks (Barkovich et al., 2005). Migration of postmitotic neurons from the ventricular zone to form the cortical plate comprises one of the most critical stages in brain development. When migration is complete, the cortex is a six-layered structure, with each layer comprising different types of neurons that form discrete connections within the CNS and perform distinct functions (O’Rourke et al., 1992). When neurons reach their destination, they stop migrating and order themselves into specific “architectonic” patterns in brain development (Fig. 21.1A). Understanding this complex process has progressed based on studies of human malformations and mouse models with deficient neuronal migration, particularly the malformation known as lissencephaly (LIS).

The term *lissencephaly*, derived from the Greek words *lissos* meaning smooth and *enkephalos* meaning brain, is a neuronal migration disorder characterized by absent (agyria) or decreased (pachygyria) convolutions, producing a smooth cere-
The cytoarchitecture consists of four primitive layers including an outer marginal layer, which contains Cajal-Retzius neurons (layer I), a superficial cellular layer, which contains numerous large and disorganized pyramidal neurons (layer II) corresponding to the true cortex, a variable cell-sparse layer (layer III), and a deep cellular layer composed of medium and small neurons, which extends more than half the width of the mantle (layer IV) (Kato and Dobyns, 2003). The white matter, which is severely reduced in volume, occasionally contains individual neurons or collection of neurons forming heterotopia.

Mechanisms by which cell migration into the cortical plate stops at the appropriate location have been elucidated through the characterization of the Reeler mutant mouse (Caviness and Sidman, 1973). In this animal model, the cortical pattern is

![Fig. 21.1](image-url)