

European Forum on Epilepsy
Research
25th - 27th May 2013
Dublin, Ireland
www.epilepsyresearcheurope.org

THE LEADING VOICES IN THE
EPILEPSY COMMUNITY ...

...AROUND ONE TABLE



Epilepsy and early brain development

Heiko J. Luhmann

Institute of Physiology, University Medical Center of Mainz, Germany



UNIVERSITÄTS**medizin.**
MAINZ

Epilepsy and early brain development

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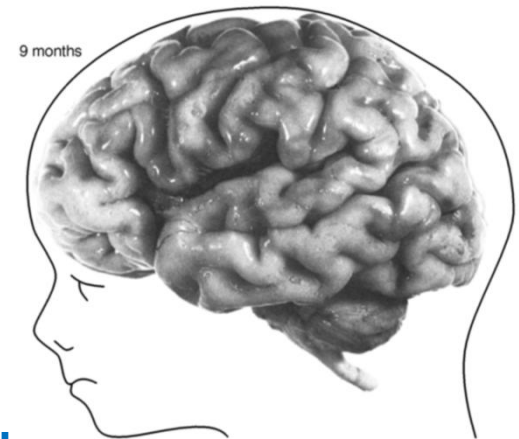
UNIVERSITÄTSmedizin.
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4 months
before birth

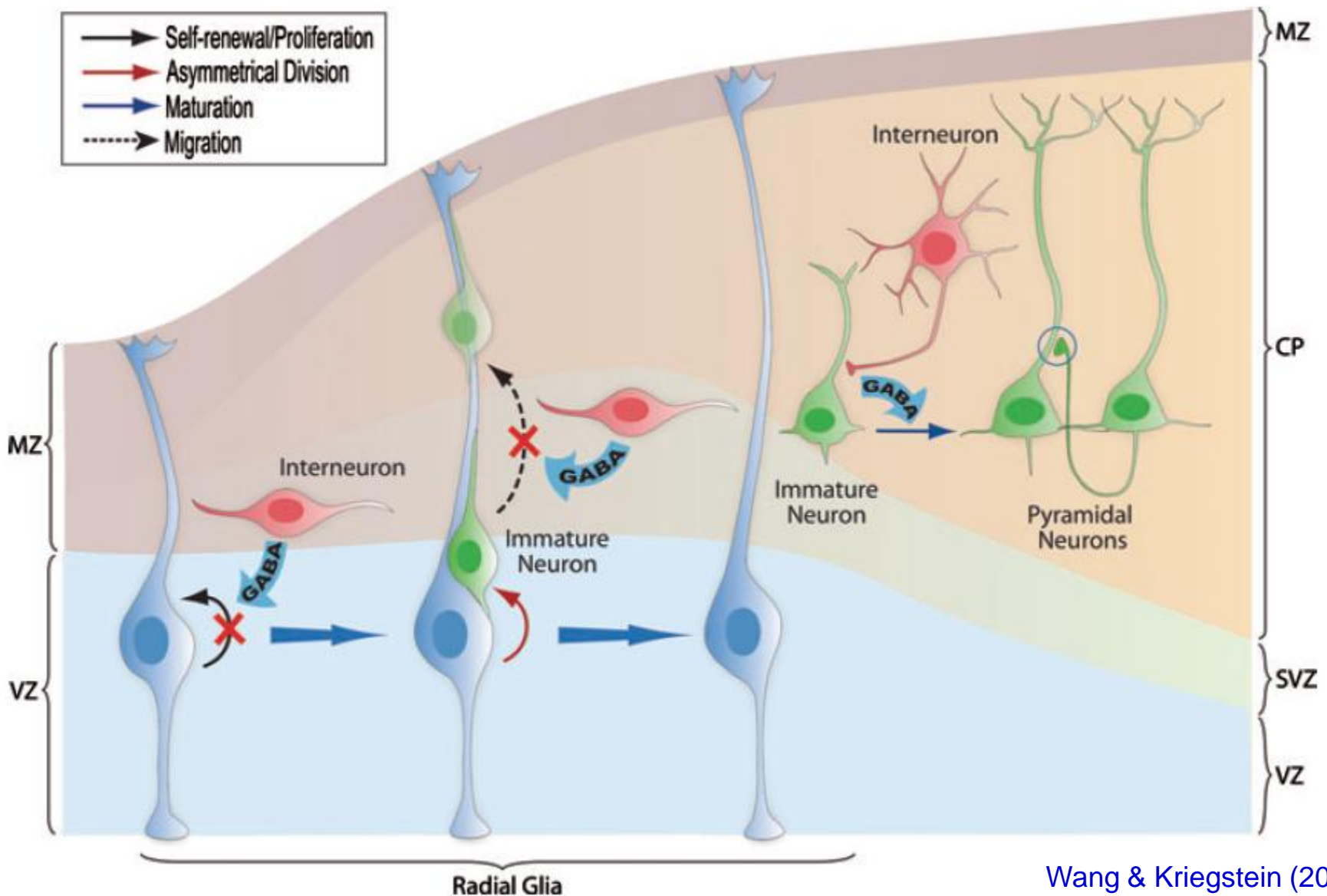


- cells are generated and dying,
- neurons migrate and differentiate,
- connections are made and removed,
- networks are formed and reorganized,
- neurotransmitters change their function.

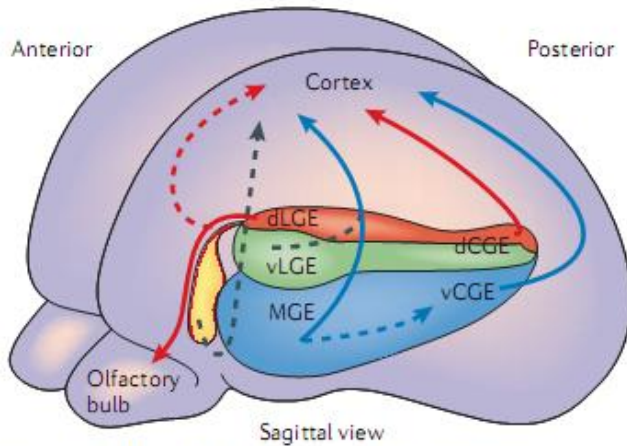
birth



1. Birth of neurons - regulated by neurotransmitter GABA (neurogenesis, stem cell therapy)

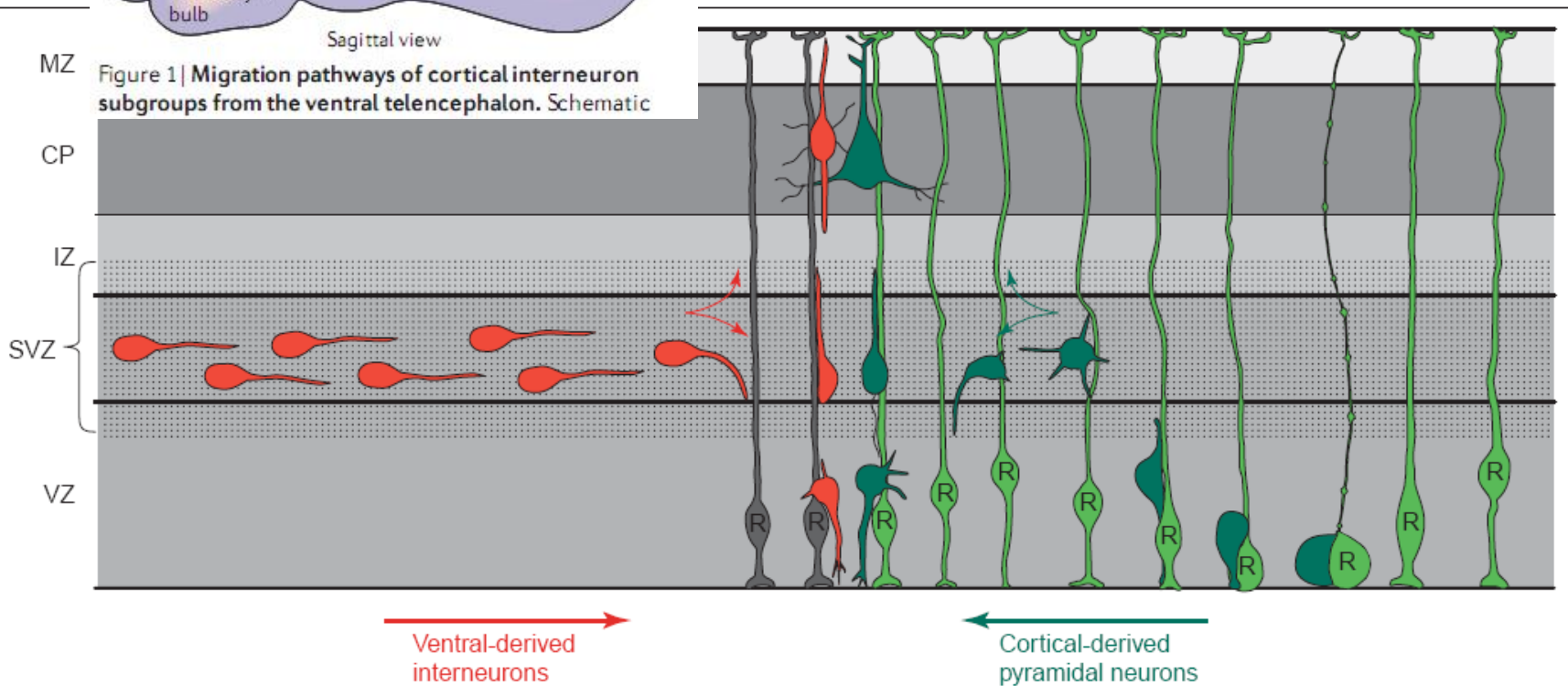


2. Neuronal migration

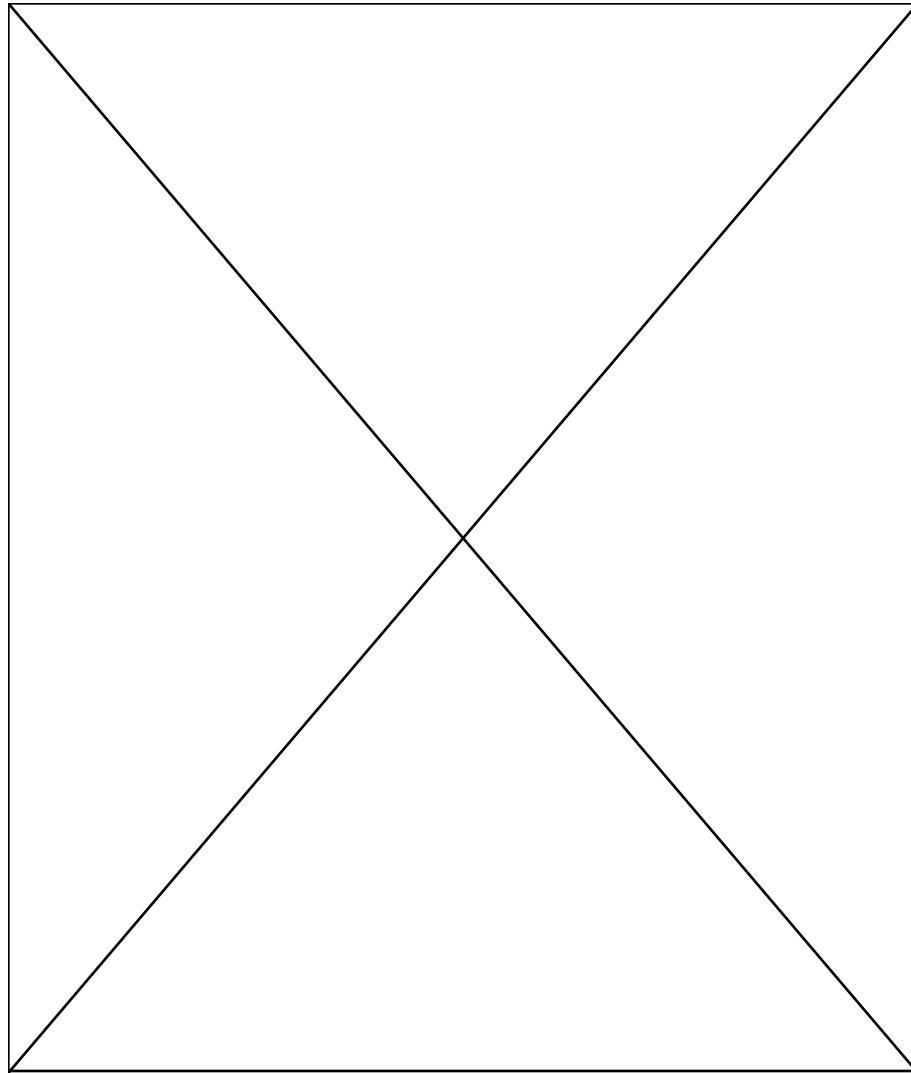


Wonders & Anderson (2006)

Kriegstein & Noctor (2004)

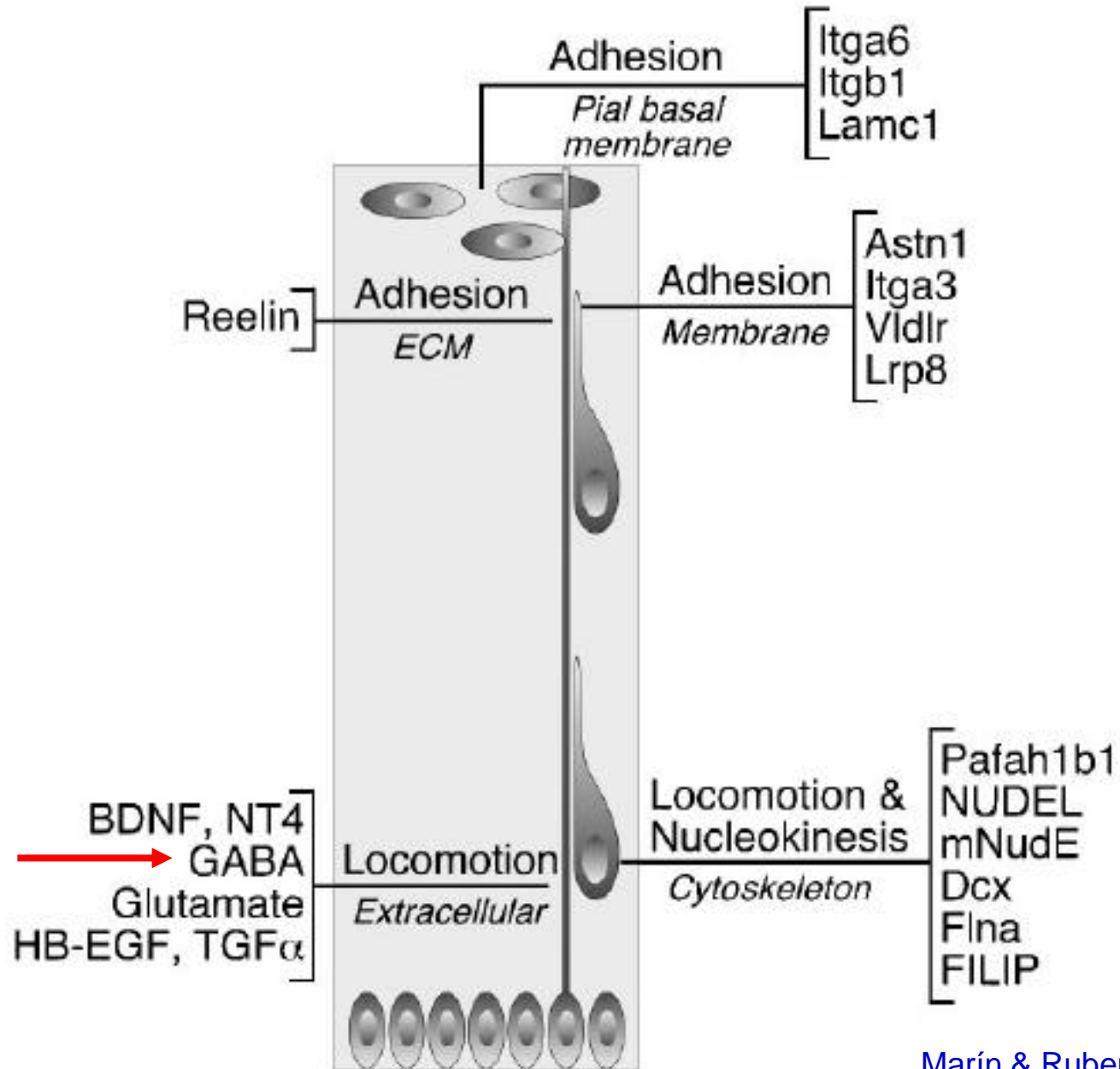


Cell migration may be disturbed not only in epilepsy, but also in other neurological and neuropsychiatric disorders

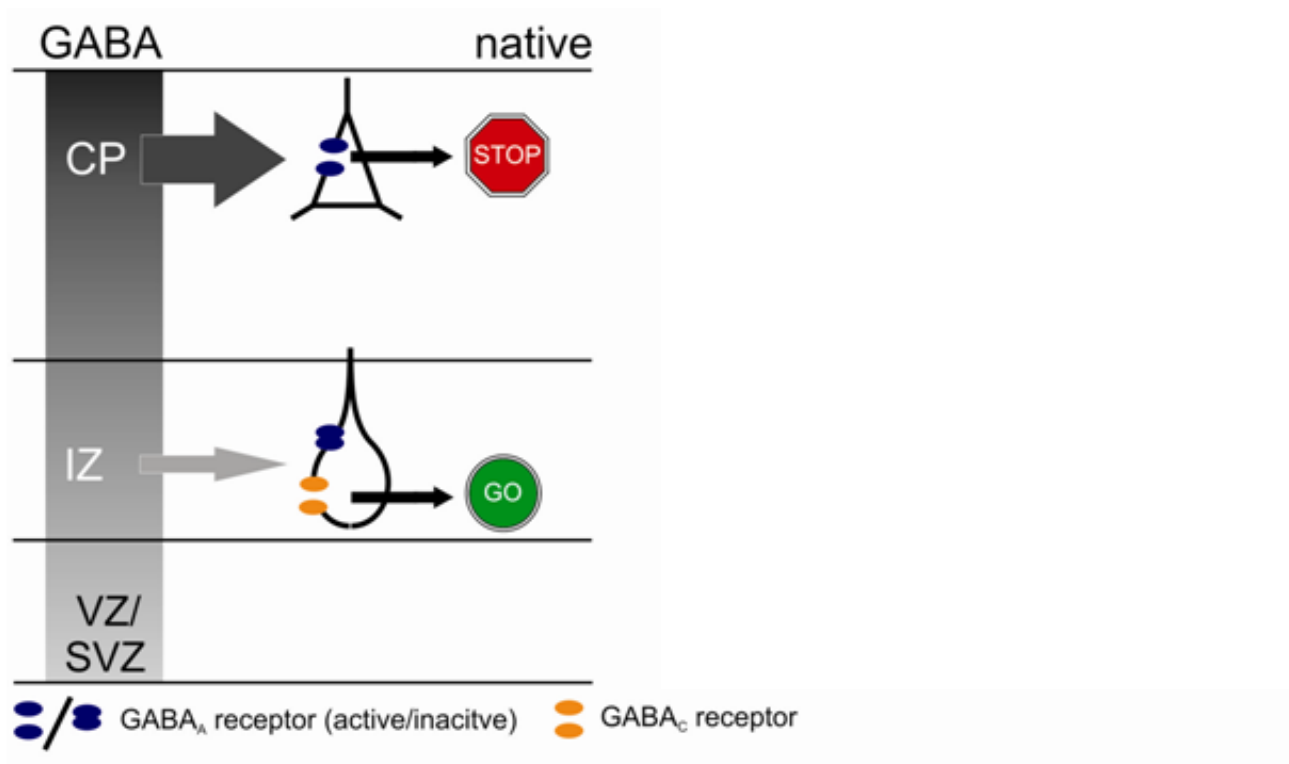


(from P. Rakic, Yale University)

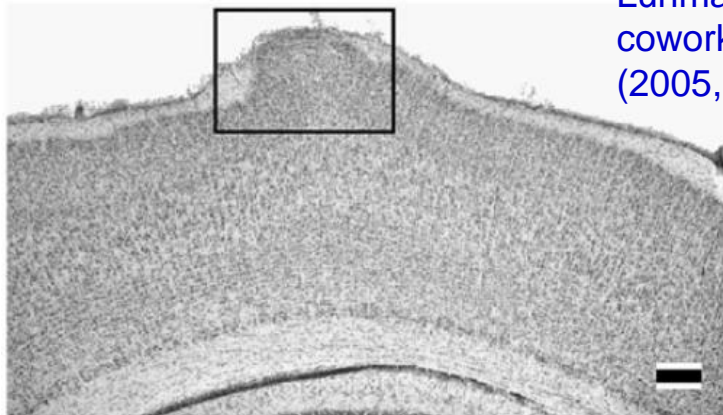
Cell migration is controlled by many factors



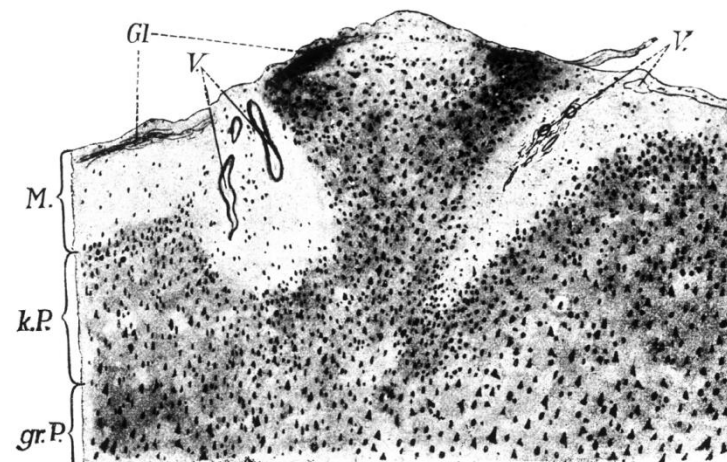
Cell migration is regulated by neurotransmitters as GABA



GABA modulation



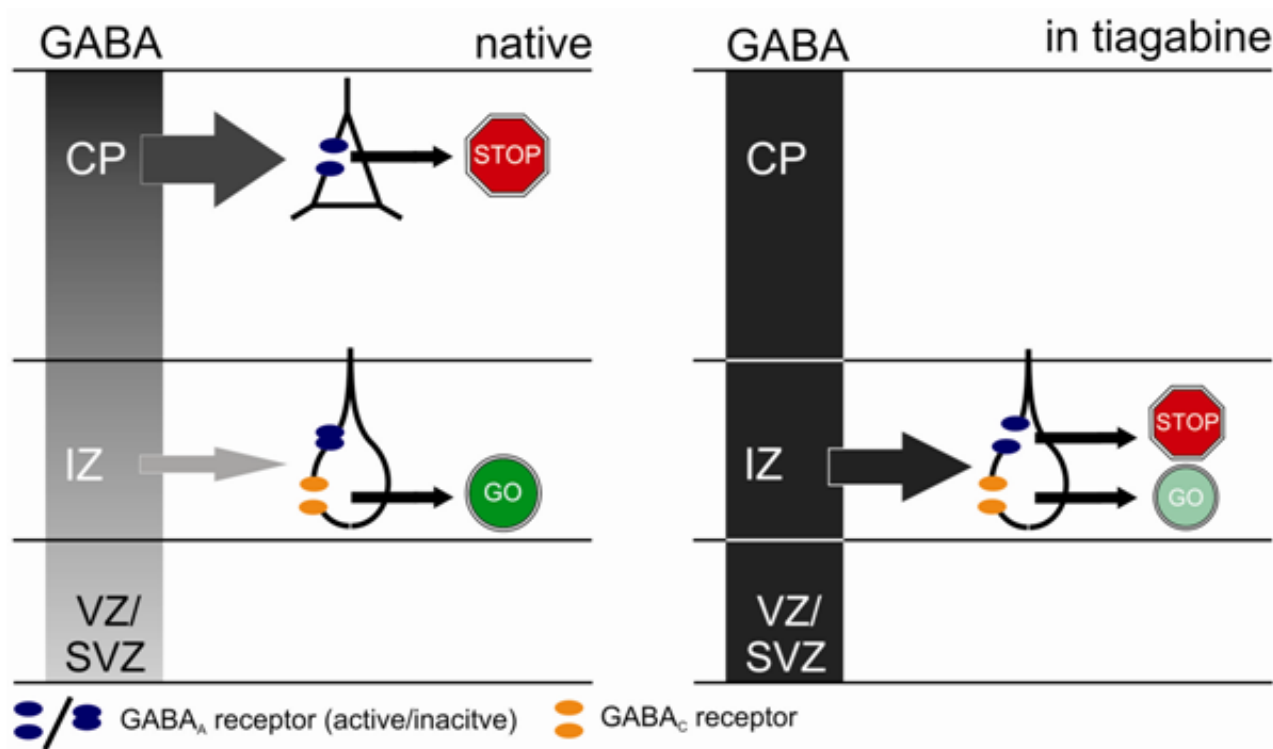
Luhmann & coworkers (2005, 2007)



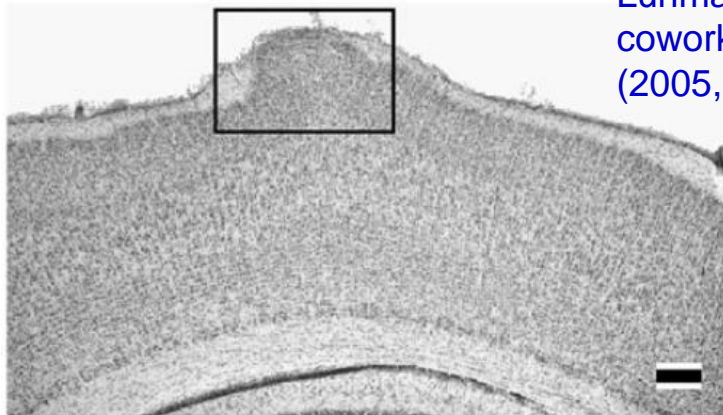
Virchow (1867)

Fig. 4.

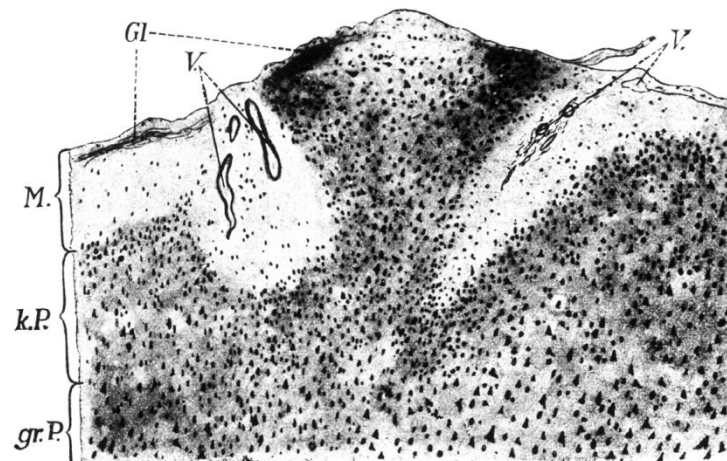
Cell migration is regulated by neurotransmitters as GABA



GABA modulation



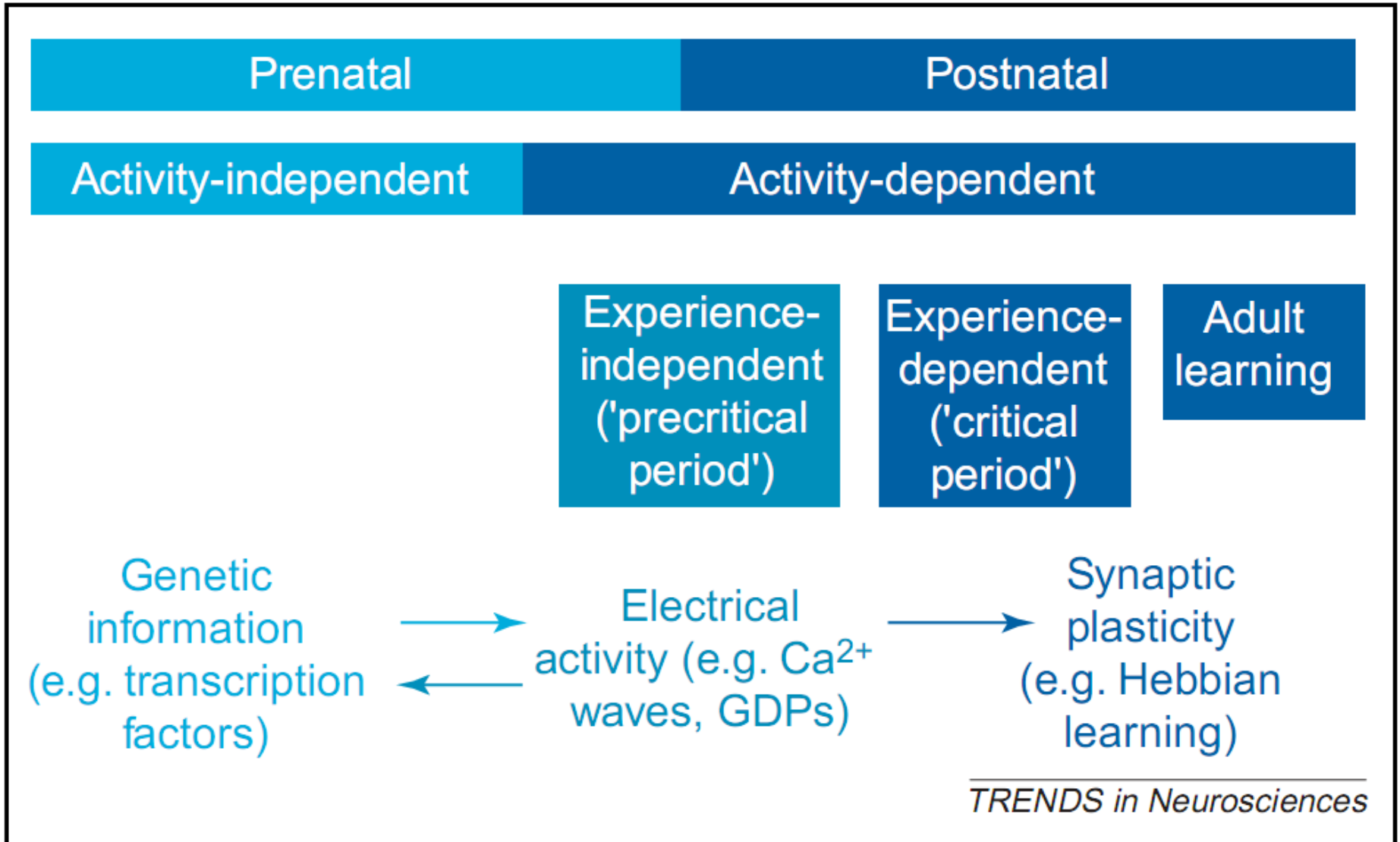
Luhmann & coworkers (2005, 2007)



Virchow (1867)

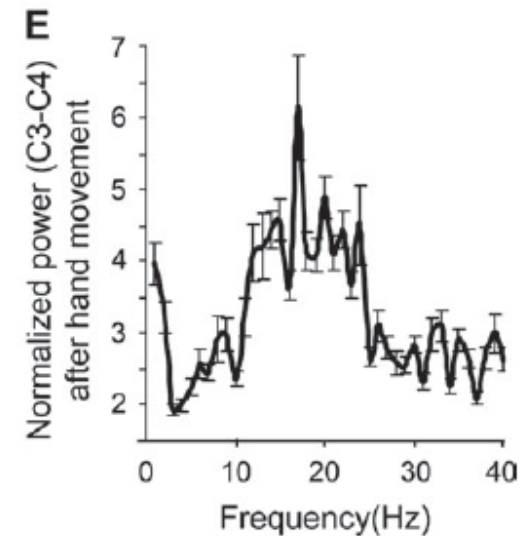
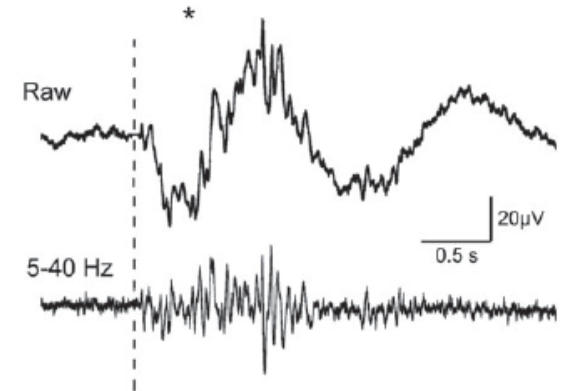
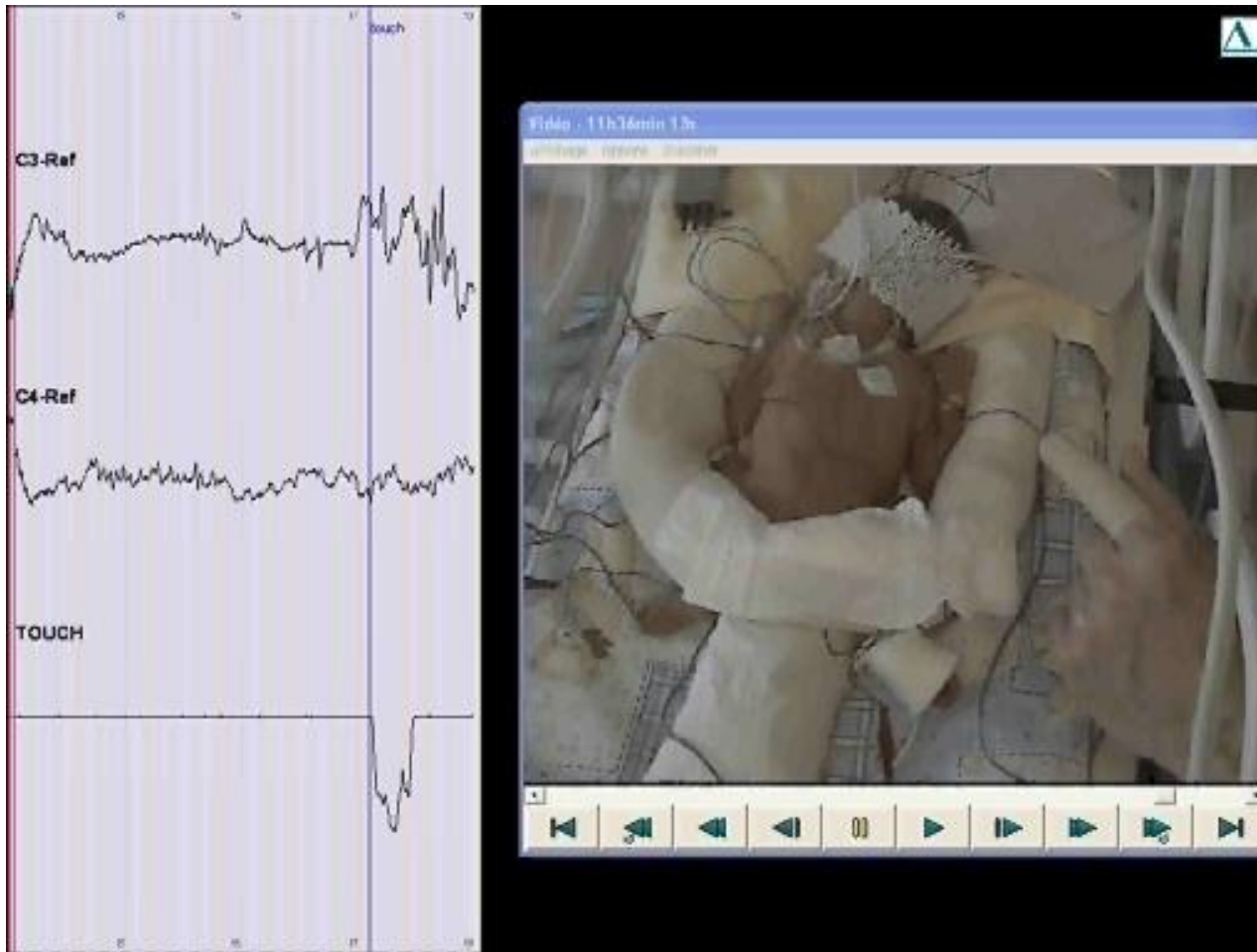
Fig. 4.

3. Network activity



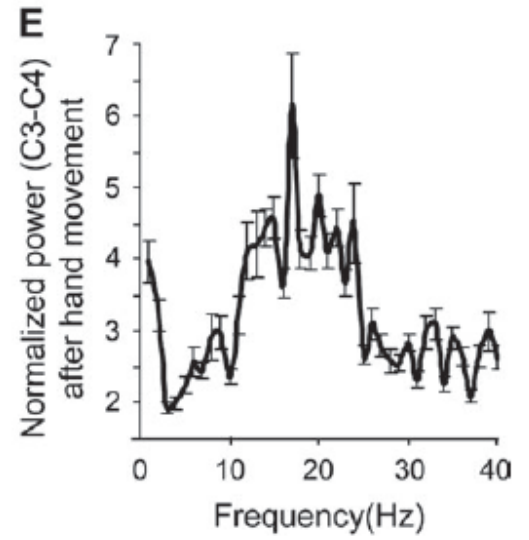
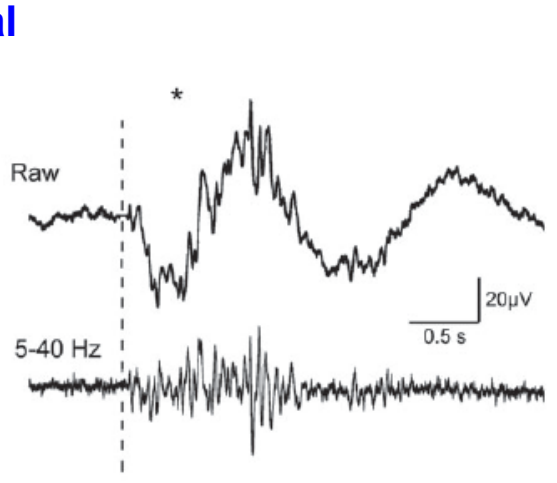
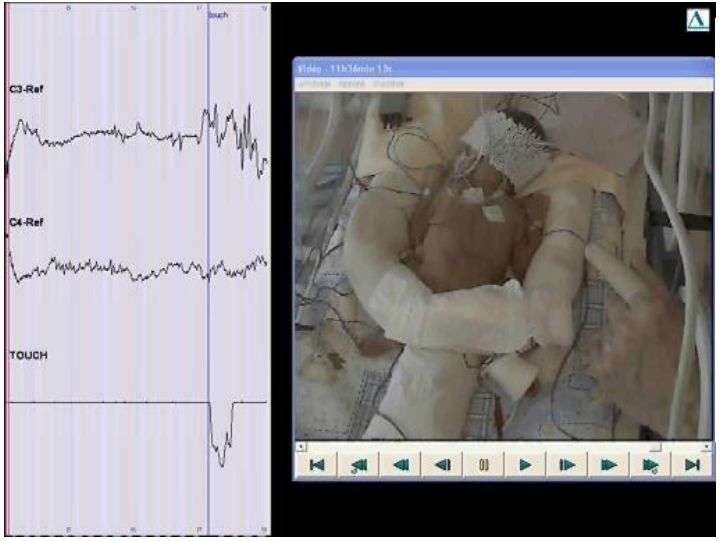
The very immature brain is very active !

age: ca. 6 months postconceptional



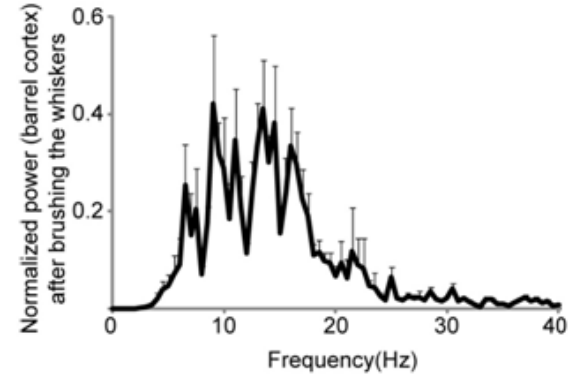
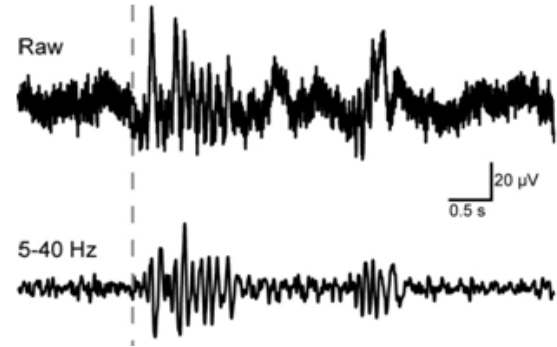
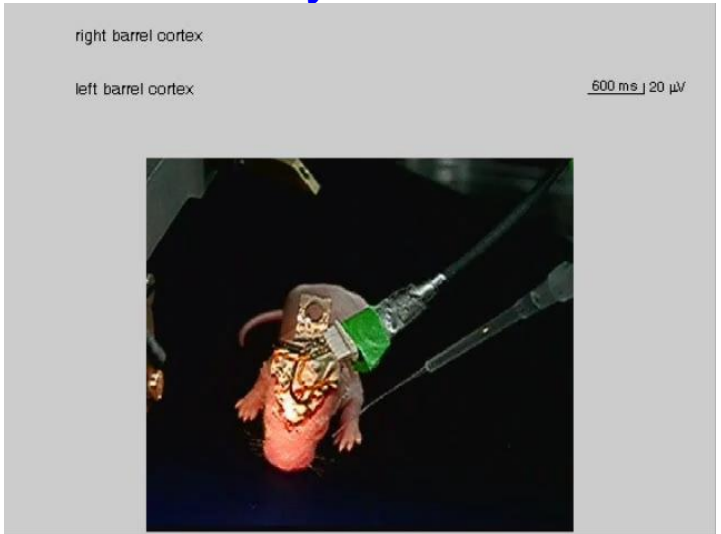
Animal models are most valuable, important and necessary !

age: ca. 6 months postconceptional



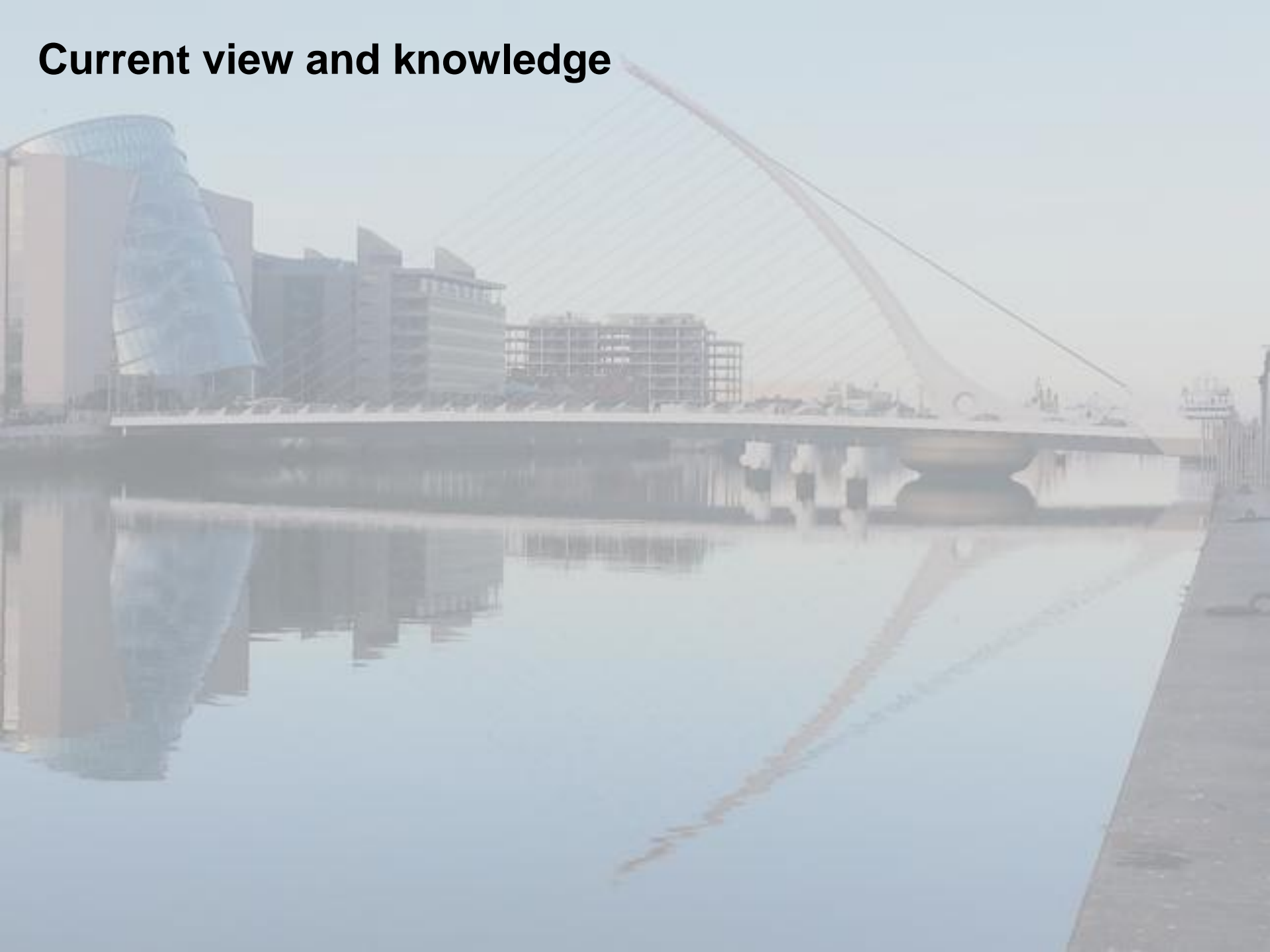
Milh, ..., Ben-Ari, Khazipov (2009) *Cerebral Cortex*

3 days old rat



Luhmann and coworkers, unpublished

Current view and knowledge



Current view and knowledge

- The young brain is NOT a small adult brain !
- By studying epilepsy we get further insights into normal brain development and into other brain disorders (e.g. autism).
- We constantly develop new methods and improve existing techniques in basic and clinical research to understand developmental processes in the brain, both at the genetic / molecular level as well as at the network / whole brain level.

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Future and open questions

- Why is the immature brain more vulnerable to develop epilepsy?
- What are the causes of early and late-onset epilepsy?

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Future and open questions

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EU-wide interdisciplinary interactions and cooperations in basic and clinical research and translational approach between both fields.

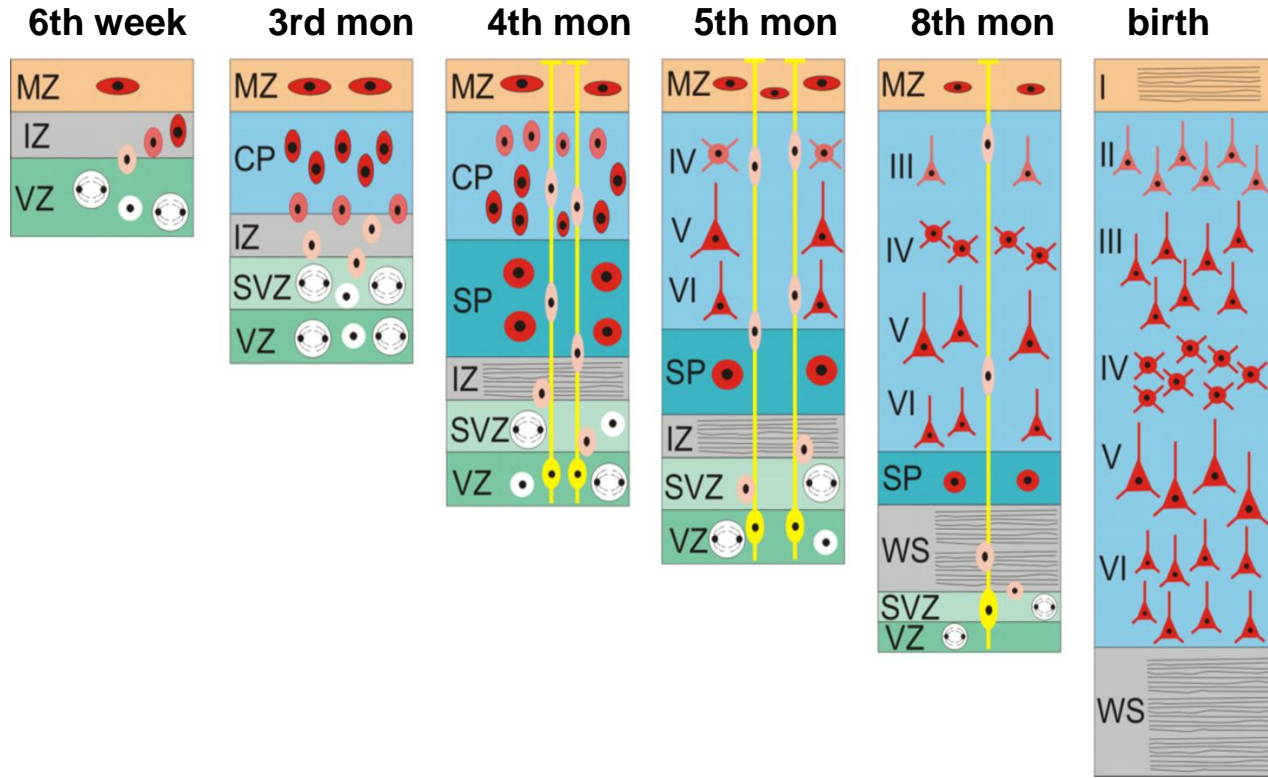
"That's our job to bridge that gap."

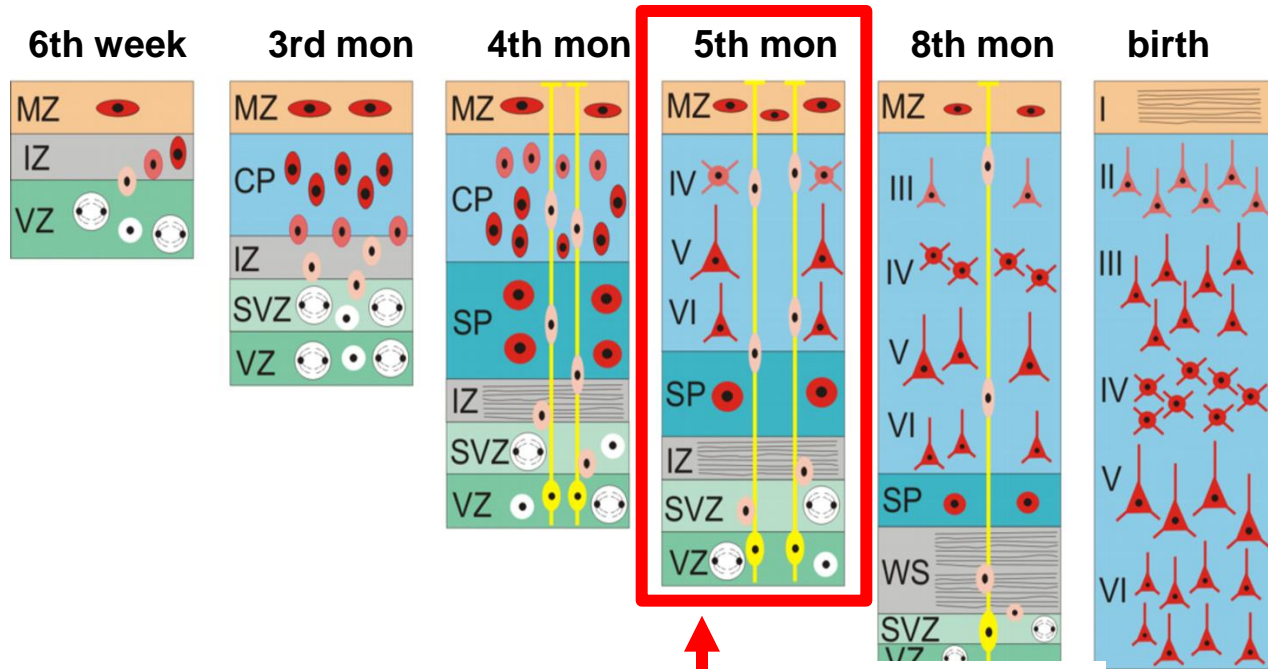
Nikki Saarsteiner, Dublin, 25th May 2013

**Thank you for
your interest,
your attention and
your support !**

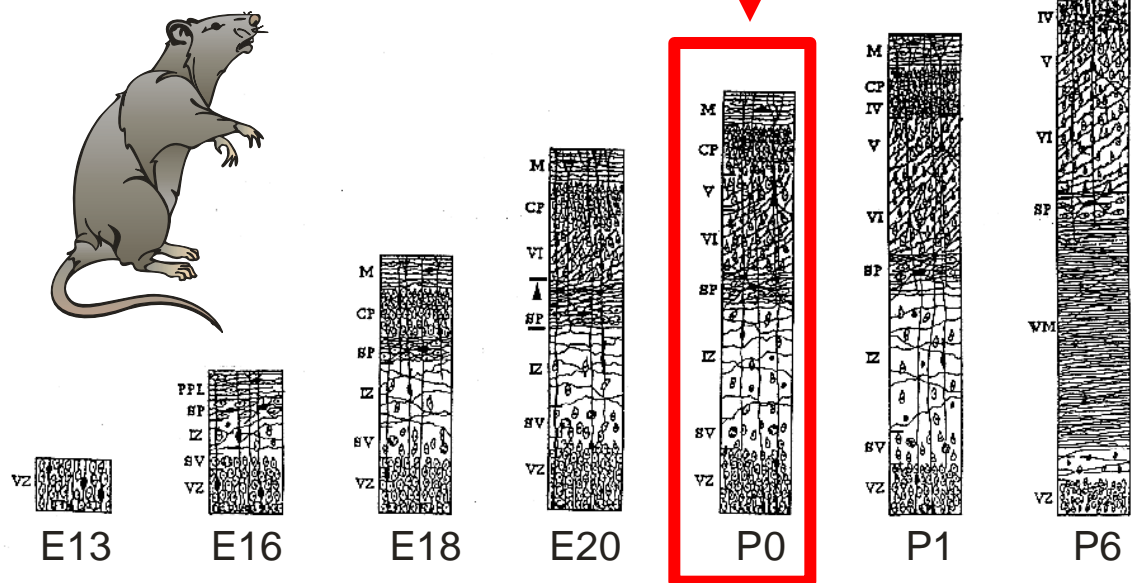


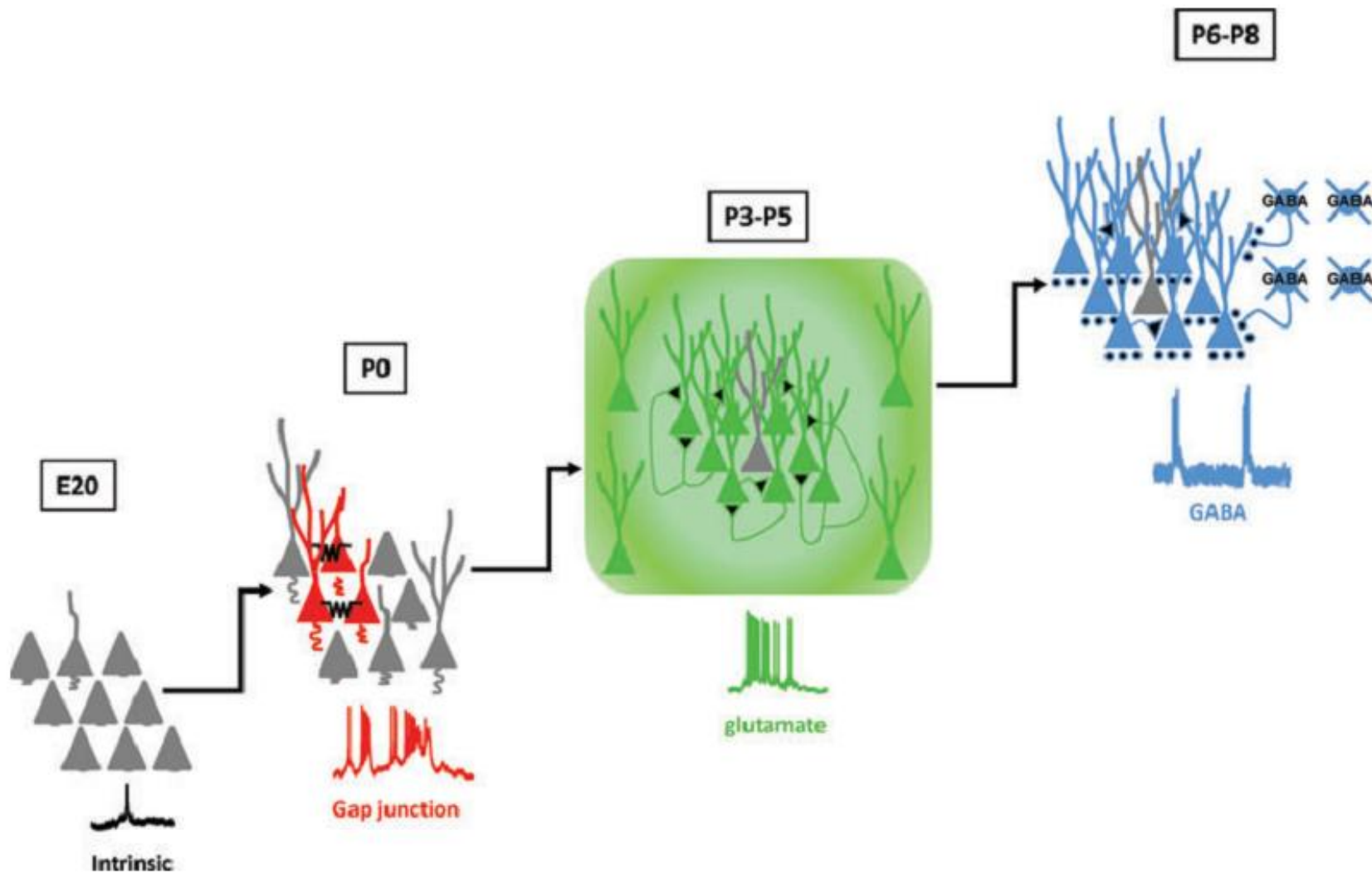
Development of cortical layers during prenatal human development

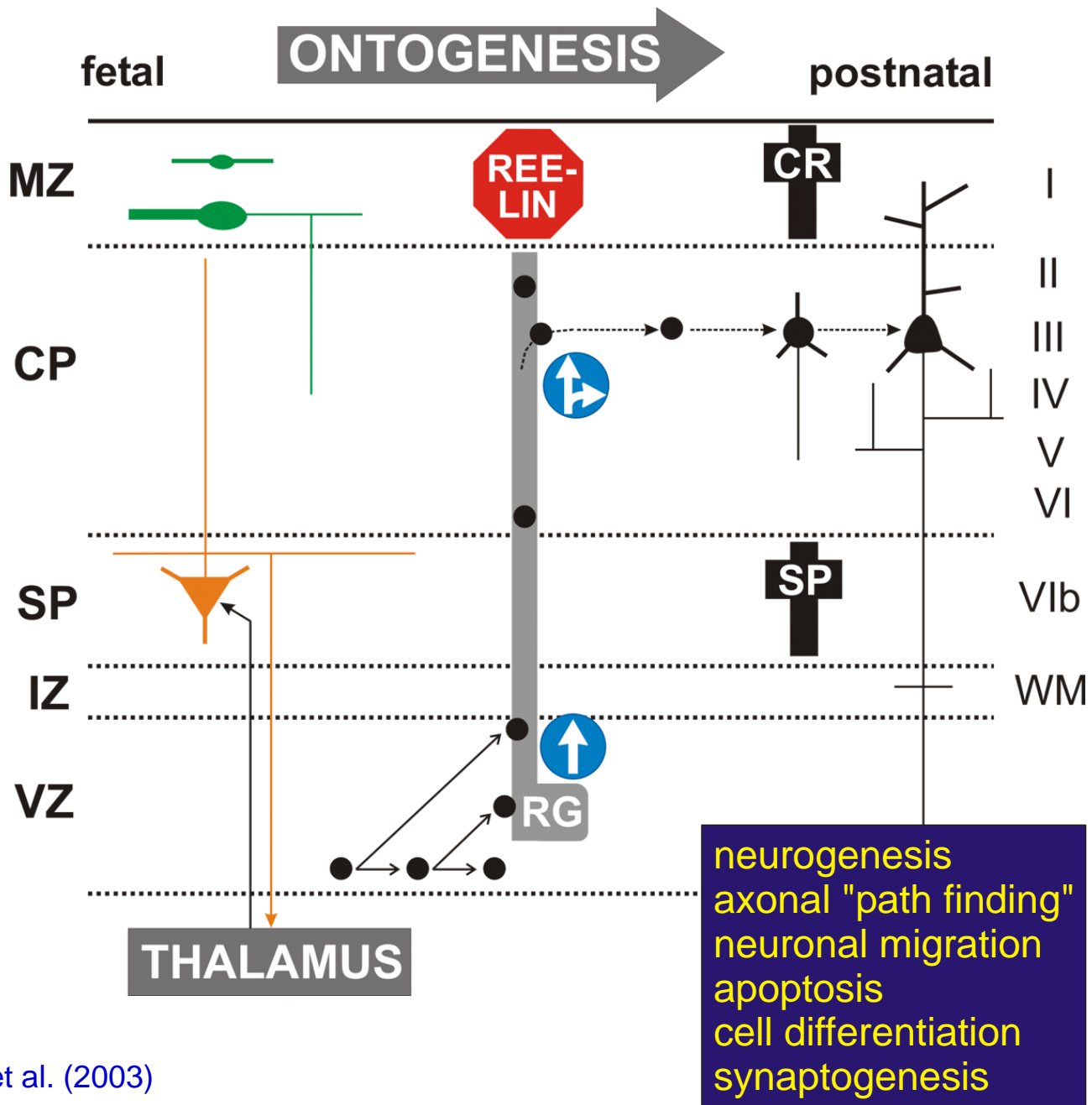




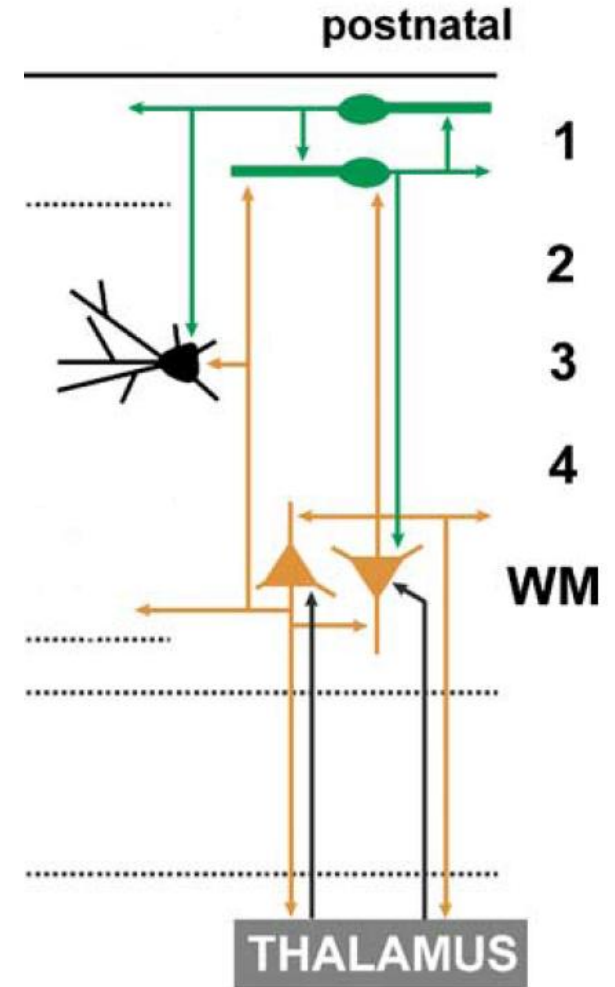
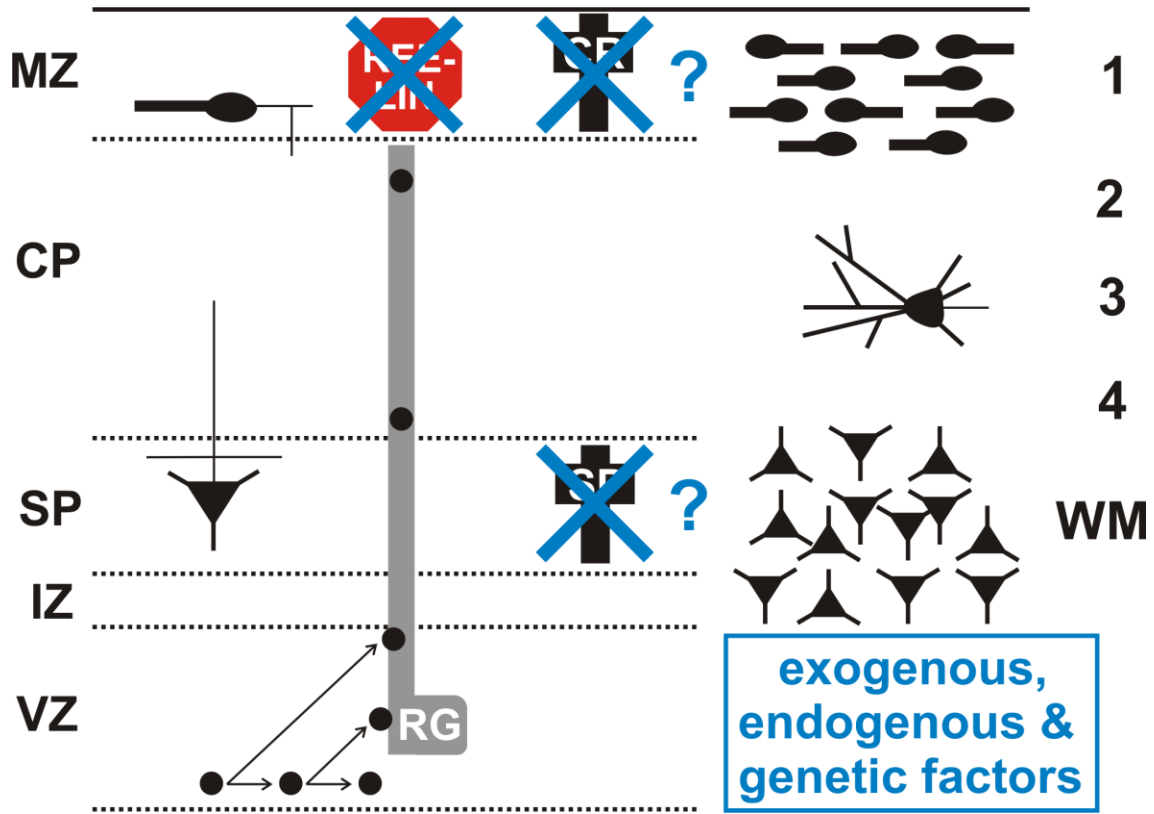
Development of rat cerebral cortex
(modified from Kageyama & Robertson, 1993)



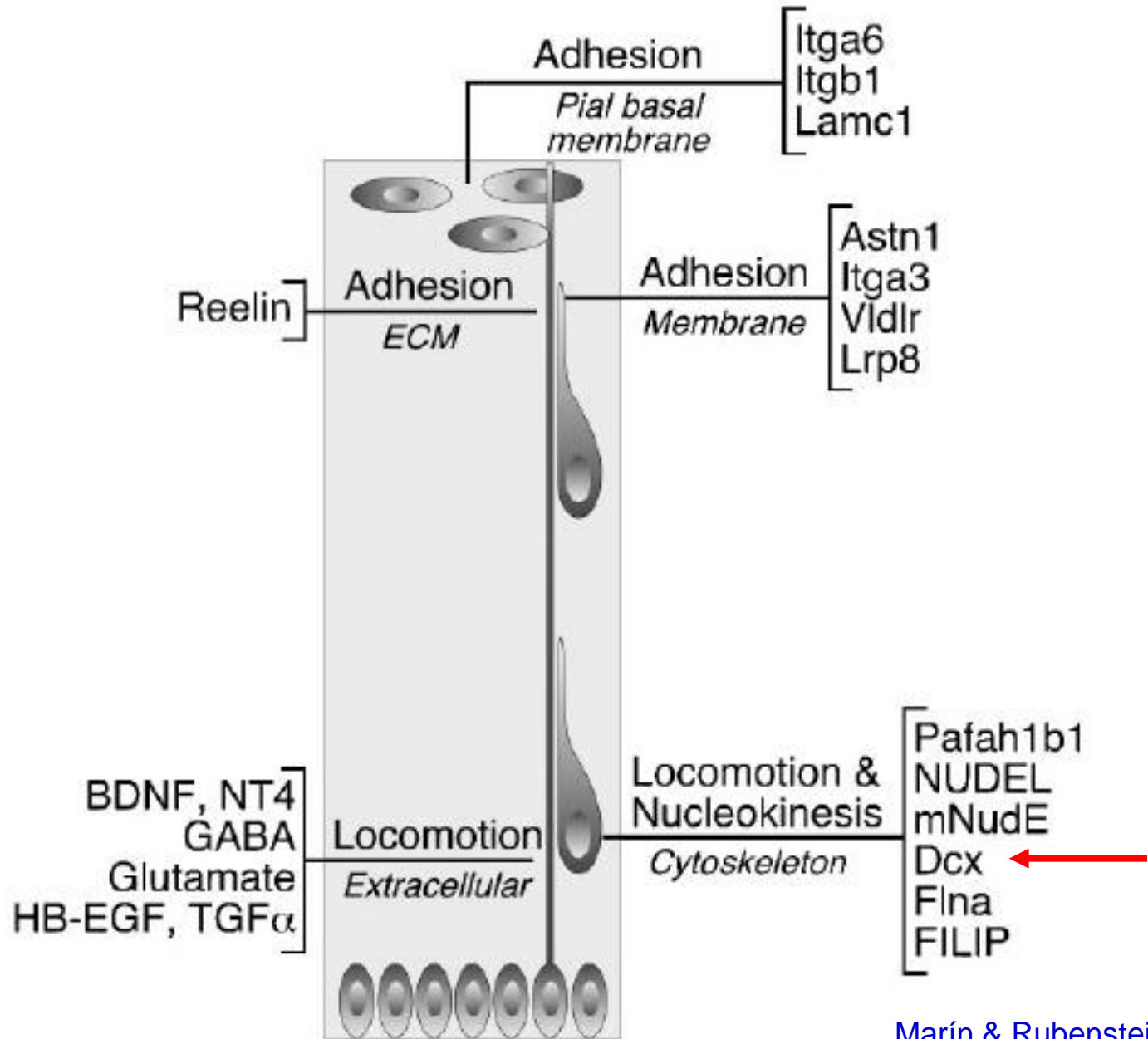




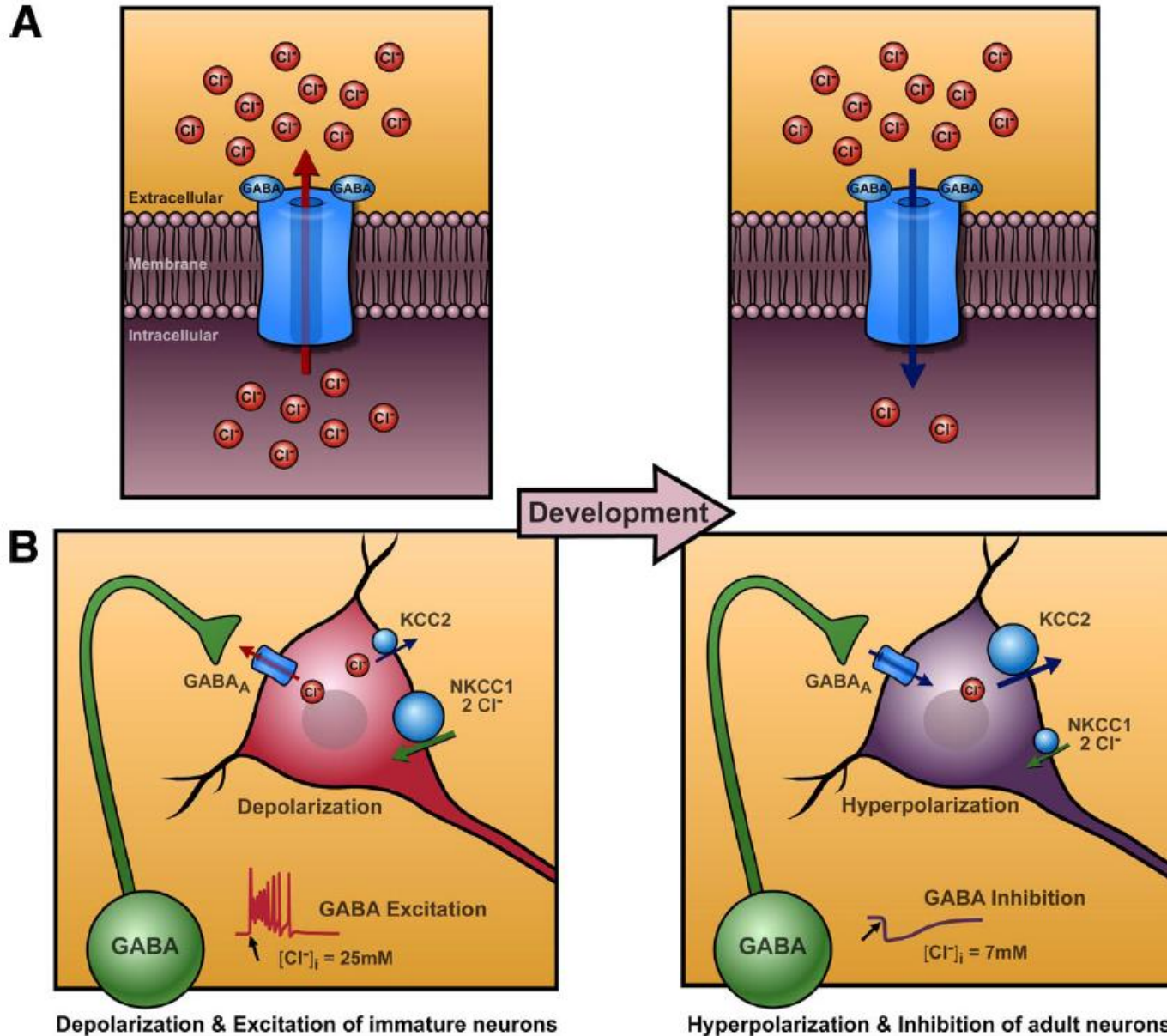
Developmental disorders of the cerebral cortex



Cell migration is also regulated by neurotransmitters



Change in GABA function during early development !



Spontaneous Epileptic Manifestations in a DCX Knockdown Model of Human Double Cortex

Damien Lapray¹, Irina Y. Popova², Jennifer Kindler¹, Isabel Jorquera², H el ene Becq², Jean-Bernard Manent², Heiko J. Luhmann¹ and Alfonso Represa²

